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CALORIMETRIC DETERMINATION OF HEATS
OF PROTONATION

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDENTS
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

BY

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The undersigned certify that they have read, and
recommend to the Faculty of Graduate Studies for acceptance,
a thesis entitled:

CALORIMETRIC DETERMINATION OF HEATS
OF PROTONATION

submitted by Donald Robert Weir, in partial fulfilment of
the requirements for the degree of Doctor of Philosophy.

ABSTRACT

A calorimeter, which was convenient to use, was developed. It consisted of a Dewar flask, a motor driven stirrer, a thermopile as the temperature sensing device in conjunction with a recording potentiometer, and a motor driven, thermostatted buret for the introduction of one of the reactants. A statistical study of the indeterminate errors involved in a calorimetric determination is described.

The heats of protonation of twenty-two monoamines, seventeen amino acids and nine diamines were determined. The enthalpy values, in conjunction with stability constants reported in the literature, were used to calculate the free energy and entropy of protonation. Differences in the thermodynamics of amino protonation has been discussed in terms of solvation and non-solvation effects. It has been concluded that enhancement of water structure formation is responsible for some of the differences found and further that the unprotonated species principally cause structure formation in the solvent.

The heats of protonation of these compounds have been compared with the stability of their metal complex compounds and a direct relationship has been found.

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I. INTRODUCTION

A. General

In the last fifteen years there has been a renewed interest in inorganic chemistry which has manifested itself in the study of the kinetics and thermodynamics of coordination reactions and in the study of organometallic and non-metallic compounds.

The increased activity in the study of coordination reactions has been largely due to the expansion and improvement of analytical techniques. The developments which have been of particular value are those which can be used in situ, e.g. the glass electrode, polarography, spectrophotometry, nuclear and paramagnetic resonance.

The emergence of certain theories and methods have also added to the impetus of the resurgence of inorganic chemistry. Ligand Field Theory (1), in particular has made it possible to correlate many properties of coordination compounds with the electronic structure of the metal ion, e.g. absorption spectra, magnetic behaviour, stability and stereochemistry. Reaction kinetics methods, (2) developed mainly in the field of organic chemistry, have been profitably applied to reactions of coordination compounds (3). The Bjerrum titration (4) has allowed the determination of step-wise stability constants that were previously difficult or impossible to obtain.

The behaviour of solutes and solvents and their influence one upon the other has received considerable attention in recent years, for the very good reason that the majority of

the chemical reactions that have been studied take place in solution. A number of hypotheses have emerged to explain the observed phenomena. (5, 6, 7)

B. Thermodynamics

Knowledge of the thermodynamic data of reactions is invaluable in the interpretation and prediction of chemical phenomena. The most useful expressions are those derived from the definition of the Gibbs' free energy:

$$F = H - TS, \quad \text{I.}$$

where F is the Gibbs' free energy, H is the enthalpy, T is the absolute temperature, and S is the entropy.

The Gibbs' free energy is a measure of the propensity of a system to progress from the initial to final state. The enthalpy change is a measure of the changes in bond strengths and other attractive forces in the system. The entropy change is a measure of the change in randomness of the system.

The equilibrium constant, K , of a reaction is related to the free energy change by the following expression

$$-RT \ln K = \Delta F^\circ = \Delta H - T \Delta S^\circ. \quad \text{II.}$$

If the values of K are available over a range of temperatures, the enthalpy change, ΔH , can be deduced from

$$\Delta H = -T^2 \frac{d}{dT} \frac{\Delta F^\circ}{T} = RT^2 \frac{d \ln K}{dT}, \quad \text{III.}$$

the standard entropy change, ΔS° , from

$$\Delta S^\circ = - \frac{d \Delta F^\circ}{dT} = \frac{(\Delta H - \Delta F^\circ)}{T}, \quad \text{IV.}$$

and the change in the molar specific heat, ΔC_p , from

$$\Delta C_p = \frac{d\Delta H}{dT} = \frac{T \Delta S^0}{dT} = - \frac{T d^2 \Delta F^0}{dT^2}. \quad \text{V.}$$

If it is assumed that ΔC_p remains constant over the temperature range investigated, equations III and IV can be integrated, giving

$$\Delta H = \Delta H_0 + \Delta C_p T, \quad \text{VI.}$$

$$\Delta S = \Delta S_0 + \Delta C_p \ln T, \quad \text{VII.}$$

$$\ln K = \frac{\Delta H_0}{RT} + \frac{\Delta C_p \ln T}{R} + \frac{(\Delta S_0 - \Delta C_p)}{R}. \quad \text{VIII.}$$

Equation VIII is a three constant equation of the form

$$\ln K = \frac{A}{T} + B \ln T + C,$$

and the three constants can be evaluated if K is known with sufficient accuracy over a range of temperature. It is readily apparent from the above relationships that an accurate knowledge of the stability constants of reactions is important.

Guldberg and Waage first considered chemical equilibria on a quantitative basis about a century ago. (8). In 1877, van't Hoff derived the equation for what is commonly known as the law of mass action. Ostwald, in 1889, combined Arrhenius' theory of electrolytic dissociation with the Guldberg and Waage treatment of chemical equilibria to determine the first dissociation constant of 215 carboxylic acids using conductivity measurements. The first calculation of the second dissociation step of a dibasic acid was done by Noyes in 1893 but it required independent knowledge of the first dissociation constant. The first time that the first and

second dissociation constants were determined from data where three species coexisted in solution was in 1924 by Auerbach and Smolozky.

Stability constants of metal complexes began to be reported about 1900 by Bodlander and by von Euler. In 1915, Niels Bjerrum reported the stepwise stability constants of a series of chromium (III) thiocyanato complexes. Since these complexes are very inert (kinetically), he was able to analyze the solutions for SCN^- , Cr^{+3} , $\text{Cr}(\text{SCN})^{+2}$, $\text{Cr}(\text{SCN})_2^+$, $\text{Cr}(\text{SCN})_3$, $\text{Cr}(\text{SCN})_4^-$, $\text{Cr}(\text{SCN})_5^{2-}$, and $\text{Cr}(\text{SCN})_6^{3-}$ (9).

Although a number of experimental and computational techniques were developed before 1940, it was not until 1941 when Jannik Bjerrum proposed a general method for computing the stepwise stability constants of labile complexes (4) that the impulse for the widespread investigation of stability constants was planted. This method combined with the invention of the glass electrode caused a phenomenal growth in the field. Knowledge of the hydrogen ion concentration in solution is of particular value since the vast majority of ligands that will form complexes with metal ions can also be protonated in solution (10,11) and it has been shown that protonation reactions are analogous to the complex formation reactions of the same ligands (12). In recent years, there has been an extended growth in the field particularly in the use of computers to solve the complicated algebraic expressions which involve stability constants.

Rossotti and Rossotti have given a complete treatment

of the experimental and computational methods used in the determination of stability constants (13). In this treatment the authors have included over fifteen hundred references to papers dealing with the determination stability constants and related subjects.

Stability constants have generally been reported as activity quotients ("thermodynamic" stability constants) or as concentration quotients (14). The activity quotients are independent of the nature or concentration of the species in solution and are true thermodynamic quantities. However, it may be difficult to determine the thermodynamic stability constant of a species, particularly where many species coexist or where the complex formed is weak (thermodynamically), because they are determined by extrapolation to infinite dilution and thus at the more dilute concentrations, the concentration of the associated species may be of the same order of magnitude as the experimental error of the measurements. Stoichiometric stability constants are, therefore, most widely reported under defined experimental conditions. It is these constants which are generally used to calculate the free energy change of a reaction. Although these constants may not have "true" thermodynamic significance trends for a given series should be thermodynamically significant.

In the determination of the enthalpies of protonation most of the values that have been reported have been found by utilizing the temperature dependence of the stoichiometric stability constants. The temperature dependence method

method has been used successfully in the determination of the enthalpy changes of reactions of the type

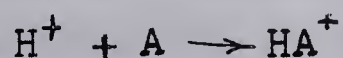


where A may be a monoamine molecule or a carboxylic acid anion. As can be seen from Table 1, the results determined from the temperature dependence of the stability constant may be in excellent agreement with the values determined calorimetrically. In other cases where a single protonation takes place the agreement is not as good as shown in Table 1 between the calorimetric and temperature dependence results that have been reported in the literature. For example Sacconi, Paoletti and Ciampolini (25) have reported the heat of protonation of piperidine as -12.19 kilocalories per mole whereas Bates and Bower (26) have reported - 12.76.

The agreement between the two methods is not nearly as good for the protonation of compounds which have two sites available for protonation as it is for monofunctional compounds. Ethylenediamine is the simplest amine that forms chelate rings with metal ions, and for this reason it has been studied in detail. In Table 2, the results of several workers are tabulated. It can be seen that the results reported show marked variation. The values determined from the temperature dependence of the stoichiometric stability constants were found to be consistently lower than those determined calorimetrically. Even the values calculated from the carefully obtained data of Cotton and Harris, differ from the

TABLE 1.

COMPARISON OF ENTHALPY DATA DETERMINED FROM THE TEMPERATURE DEPENDENCE OF THE STABILITY CONSTANT AND BY CALORIMETRY FOR REACTIONS OF THE TYPE:



BASE	$-\Delta H$	METHOD	REFERENCE
	kilocalories/mole		
Acetate	- 0.11	temperature dependence	15
	- 0.08 (0.03M)	calorimetry	16
Ammonia	12.478	temperature dependence	17
	12.425	temperature dependence	18
	12.49	calorimetry	19
	12.51*	calorimetry	This work
	12.57 (0.015M)	thermometric titration	20
Ethanolamine	12.079	temperature dependence	21
	12.07 (0.07M)	temperature dependence	22
	12.10 (0.015M)	thermometric titration	20
Trimethylamine	8.83	temperature dependence	23
	8.83	temperature dependence	24
	8.91 (0.15M)	calorimetry	This work

* Extrapolated to infinite dilution (see Figure 19.).

TABLE 2.

COMPARISON OF ENTHALPY DATA DETERMINED FROM THE TEMPERATURE DEPENDENCE OF THE STABILITY CONSTANT AND BY CALORIMETRY FOR THE STEPWISE PROTONATION OF ETHYLENEDIAMINE.

$-\Delta H_1$	$-\Delta H_2$	METHOD	REFERENCE
kilocalories/mole			
11.82	10.87	temperature dependence	27
11.5	10.3	temperature dependence	28
11.4*	9.8*	temperature dependence	29
8.7*	8.7**	temperature dependence	30
11.91	10.94	calorimetry	31
12.20	10.60	calorimetry	32
12.28	10.62	calorimetry	this work
12.38	10.83	thermometric titration	20

* calculated from the stability constants reported at 0 and 49.1° centigrade

** calculated from the stability constants reported at 0 and 25° centigrade

average of the calorimetrically determined results by 7%.

In Table 3 are tabulated some enthalpy data reported in the literature for the chelation of nickel (II) by ethylenediamine. Here again the data determined from the temperature dependence of the stability constants are in fairly serious disagreement with those determined calorimetrically.

The difference between the temperature dependence results and the calorimetric results may be due to a combination of the following factors. Some of the enthalpy values determined from the temperature dependence of the stability constant have been calculated from data obtained at only a few different temperatures (some using only two temperatures (34)). This leads to rather imprecise values of ΔH , e.g. the 95% confidence limits for ΔH_{1-3} reported by Cotton and Harris for the nickel-ethylenediamine reaction are 2.8 kilocalories per mole or about 12%. In most of the temperature dependence studies it has been assumed (28, 29) that ΔC_p is roughly constant, which may be a valid assumption in some cases but certainly not for all reactions (38) (with the lack of data at more than two or three temperatures it would be difficult to evaluate ΔC_p in any event). Since the exact meaning of pH at temperatures other than 25° centigrade is imperfectly understood (29), there is a distinct possibility that its use may give rise to a systematic error in the value of the stability constants determined at temperatures other than 25°, thus there

TABLE 3.

COMPARISON OF ENTHALPY DATA DETERMINED FROM THE TEMPERATURE DEPENDENCE OF THE STABILITY CONSTANT AND BY CALORIMETRY FOR THE REACTIONS OF ETHYLENEDIAMINE WITH NICKEL (II) ION.

$\text{Ni}^{++} + \text{en} \rightarrow \text{Ni(en)}^{++} + \Delta H_1$ $\text{Ni}^{++} + 2\text{en} \rightarrow \text{Ni(en)}_2^{++} + \Delta H_{1-2}$ $\text{Ni}^{++} + 3\text{en} \rightarrow \text{Ni(en)}_3^{++} + \Delta H_{1-3}$				
$-\Delta H_1$	$-\Delta H_{1-2}$	$-\Delta H_{1-3}$	MEDIUM	REFERENCE
kilocalories/mole				
		25	?	temperature dependence 33
4.8	9.1	14.0	0.5M KNO ₃	temperature dependence 34
7.9	15.7	22.9	0.15M KCl	temperature dependence 29
9.5	17.0	25.7	0	temperature dependence 28
	17.25	28.01	0.1M KCl	calorimetry 31
	18.1	25.1	0.5M KNO ₃	calorimetry 35
9.01	18.19	27.90	1M KNO ₃	calorimetry 36
8.90	18.25	28.35	1M KCl	calorimetry 37
9.05	17.90	27.40	1M KNO ₃	calorimetry 37

would also be an error in the enthalpies calculated from such data.

In the determination of the enthalpies of reaction by calorimetric methods, errors due to the above factors are eliminated since the experiments can be done at 25° C. It would therefore seem preferable to determine enthalpy data using calorimetric methods. However, relatively few enthalpy data of coordination reactions have been determined calorimetrically, but there is a growing trend towards the use of this method (39).

The principles of calorimetry are simple and have been known for a long time. Any body which can absorb the heat to be measured and whose consequent temperature change can be observed may serve as a calorimeter. The essentials of a calorimeter are provided by an open can of water, a thermometer, and a hand stirrer. However, such a crude device will produce only crude data. As the degree of precision desired is increased the physical complexity of the calorimeter increases almost exponentially.

Highly precise calorimeters have been described in the literature for about 50 years (40, 41, 42). Usually highly precise solution calorimeters require a large number of experimental readings during the short period of a calorimetric experiment. In addition most of the precision calorimeters have rather complicated mechanical designs, and as a result present manipulative difficulties.

Several treatises on the fundamentals of calorimetry

and calorimeter design have appeared over the years. Of these, six could be recommended to a novice:

1. W.P. White, "The Modern Calorimeter" (43)
2. W. Swietoslowski, "Microcalorimetry" (44)
3. J.M. Sturtevant, "Calorimetry" (45)
4. E. Calvet and H. Prat, "Microcalorimetrie" (46)
5. F.D. Rossini, ed., "Experimental Calorimetry" (47)
6. H.A. Skinner, ed., "Experimental Calorimetry" vol.2 (48)

Although there is some overlap in some of the treatments, there are enough differences in the material covered to make each valuable.

There has been the development of thermometric titration techniques during the last fifteen years (see for example the review by Zenchelsky (49)). Enthalpy data have been determined using thermometric titration techniques (20, 50). Although the data from thermometric titrations have not been as precise as the values usually determined by conventional calorimetry, it is thought that some of the techniques used in thermometric titrations could profitably be applied to conventional calorimetry.

C. Complexes

Coordination compounds have been known for over a century but it was not until about two decades ago that deep inroads began to be made in the understanding of coordination compounds and coordination reactions. There has been much work done on elucidating the factors which influence the

stability of complexes in aqueous solution.

One of the powerful new tools used to gain an understanding of the factors which influence the stability of complexes is Ligand Field Theory (1). In cases where octahedral complexing occurs (Figure 1a), the degenerate d orbitals are split into two groups as shown in Figure 1b. The magnitude of the splitting depends on the ligand and it generally increases with increasing stability of the complex for a particular metal ion with a series of ligands (51). Certain characteristics of the metal ions also influence the stability of the complexes: ionic radii, electronegativities, ligand field stabilizations, low-spin or high-spin configuration, etc. (52).

Sacconi et al (39) found that the enthalpies of formation of the complexes between divalent first transition series ions and polyamines rose from manganese (II) to copper (II) and then fell to zinc (II) as predicted from Ligand Field Theory.

There has been much interest in the effect of chelate rings on the stability of complexes. It has been found that the complexes formed between ethylenediamine and metal ions are 10 to 1000 times more stable than the corresponding complexes of ammonia (53). It has also been found that the size of the chelate ring affects the stability of the complex, i.e. a five-membered ring is more stable than a six-membered ring (29). It has been generally accepted that the chief factor causing the chelate ring induced enhancement of stability

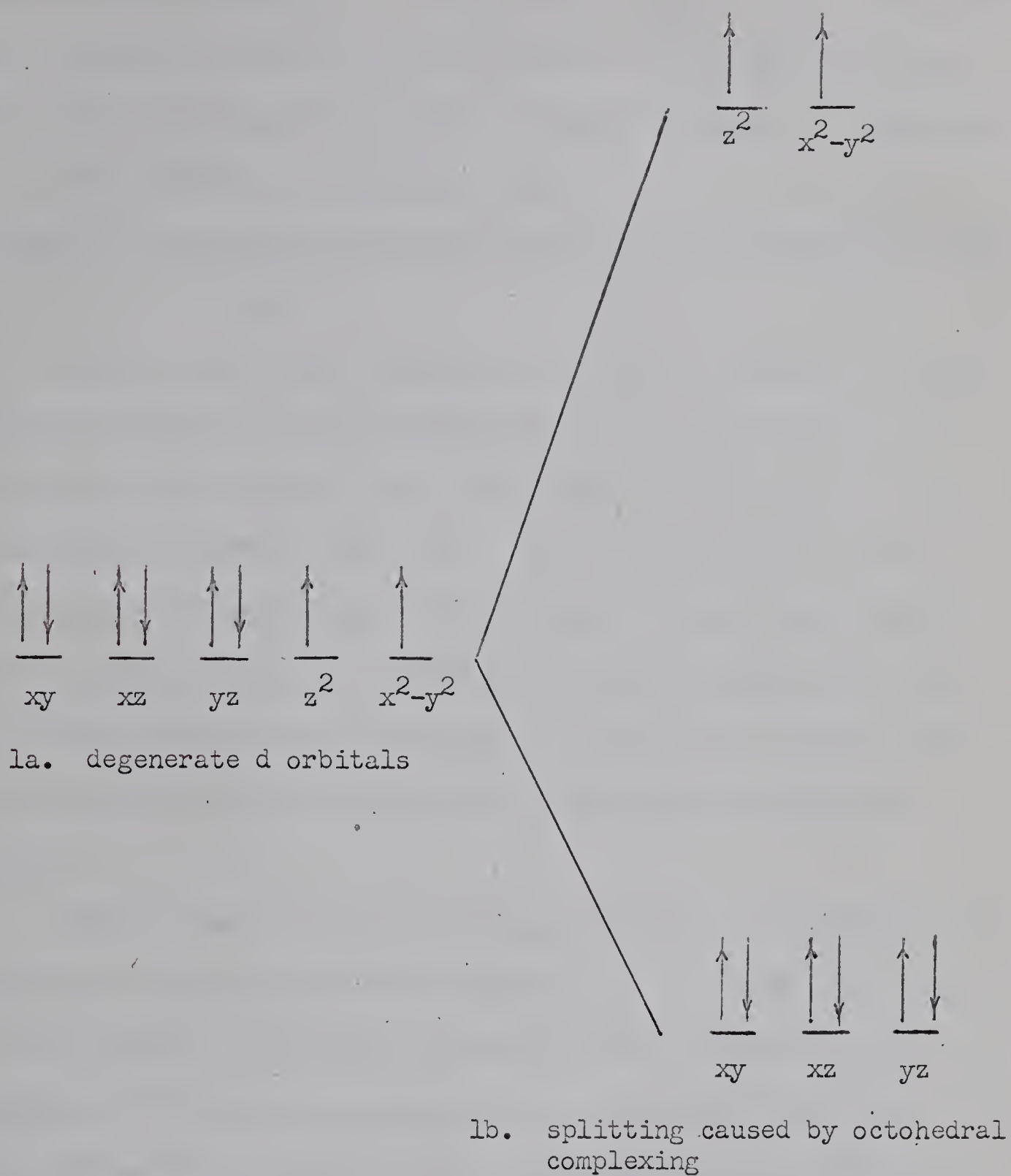
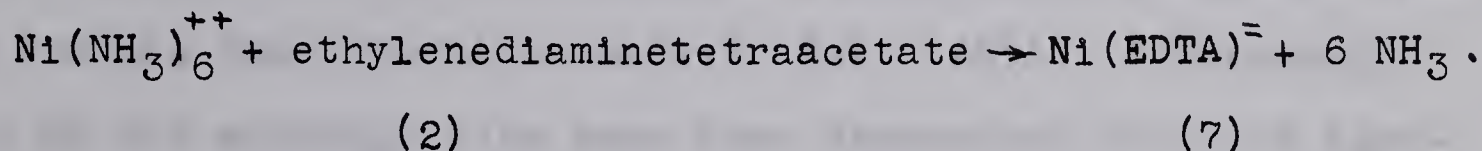


Figure 1. Relative energy levels of the d orbitals of Ni^{++} ion caused by an octahedral ligand field.

is the increased entropy of complexation (54). This has been chiefly ascribed to the fact that there is a large gain in translational entropy due to the increased number of entities formed in the chelation reaction e.g.



There have been studies in which a series of alkyl substituted ligands (ethylenediamines and amino acids) have been complexed with metal ions and their thermodynamic quantities compared (30, 34, 35, 55). The differences in the stabilities of the complexes formed were chiefly accounted for by the postulation of steric hindrance between the ligands. In the present work several of the same ligands have been protonated and their step-wise heats of protonation determined.

Since there is some analogy between protonation of a ligand and complexing of the ligand with a metal ion (12), it may be possible, once the thermodynamic functions for protonation are known, to estimate the relative roles of enthalpy and entropy terms in the formation of coordination compounds.

D. Ligands and Solvation

Although a considerable amount of data has been published on the stability of metal complexes (10, 11), most investigators have been concerned with the complex formed. The role of the ligand in going from the free form to the complexed form has not been studied in any great detail by

inorganic chemists.

Most authors who have studied the thermodynamics of ligand protonation have done so to elucidate the protonation reaction itself but not to explain coordination phenomena (see for example the references made by Bell (56)). Furthermore, most of the enthalpy data have been determined from the temperature dependence of the stability constants. More direct determinations of ΔH and ΔC_p are possible by calorimetric measurements, but not much work of sufficient accuracy has been done (16, 22, 57).

It has been stated that "In general it seems likely that free energies are more appropriate for comparison with molecular models" (than enthalpies) (58).

At absolute zero: $\Delta F_0 = \Delta H_0$, $\Delta S_0 = 0$ and $\Delta C_p = 0$. By raising the temperature

$$\Delta H = \Delta H_0 + \int_0^T \Delta C_p \, dT \quad \text{IX.}$$

$$\Delta F = \Delta H_0 + \int_0^T \Delta C_p \, dT - T \int_0^T \frac{\Delta C_p}{T^2} \, dT \quad \text{X.}$$

If a reactant is modified slightly, say by introducing a substituent, there will be changes in ΔH_0 , ΔC_p , etc. indicated by $\delta \Delta H_0$, $\delta \Delta C_p$, etc.

Then

$$\begin{aligned} \delta \Delta H - \delta \Delta H_0 &= \int_0^T \delta \Delta C_p \, dT \\ \delta \Delta F - \delta \Delta H_0 &= \int_0^T \delta \Delta C_p \, dT - T \int_0^T \frac{\delta \Delta C_p}{T^2} \, dT \quad \text{XII.} \end{aligned}$$

Bell states that there are good grounds for believing that the latter relationship will commonly be the smaller of the

two, i.e. that $\delta\Delta F$ will more closely approximate $\delta\Delta H_0$ than will $\delta\Delta H$. This can be illustrated by writing $\delta\Delta C_p$ as a power series, beginning with a term in T^3 so as to give the correct behaviour at absolute zero, i.e.

$$\delta\Delta C_p = aT^3 + bT^4 + cT^5 \dots \quad \text{XIII.}$$

This gives the result

$$\delta\Delta H - \delta\Delta H_0 = \frac{aT^4}{4} + \frac{bT^5}{5} + \frac{cT^6}{6} \dots \quad \text{XIV.}$$

$$\delta\Delta F - \delta\Delta H_0 = -\frac{aT^4}{3 \times 4} - \frac{bT^5}{4 \times 5} - \frac{cT^6}{5 \times 6} \dots \quad \text{XV.}$$

The thermodynamic functions for a reaction in a solvent, $\delta\Delta H_s$ etc., can be expressed in terms of the corresponding quantities in the gas phase by the equations

$$\delta\Delta H_s - \delta\Delta H_g = \sum H_s \quad \text{XVI.}$$

$$\text{and } \delta\Delta F_s - \delta\Delta F_g = \sum H_s - T \sum S_s \quad \text{XVII.}$$

where H_s and S_s are the heats and entropies of solution and the summation is made over all species involved in the reactions. If a species is solvated there is some exothermic heat of solvation, e.g. due to hydrogen bonding, and there is usually some change in the solvent structure. In going from the gas phase to the condensed phase (solution), there will be a loss of randomness of the system, i.e. an entropy loss. Thus generally

$$\delta\Delta H_s - \delta\Delta H > \delta\Delta F_s - \delta\Delta F. \text{ (numerically)}$$

It is clear from the above two arguments that it is probably better to use ΔF to compare molecular models, by yielding the best measure of ΔH_0 . However, there would seem to be some merit in using ΔH to elucidate factors influencing

the stability of a particular species under actual experimental conditions. This would be particularly true if the effect of the solvent on a reaction was being considered, as $\delta\Delta F$ would be expected to be small, if not indistinguishable from experimental error for a series of similar compounds. Thus $\delta\Delta H$, although not the best measure of $\delta\Delta H_0$, should be a good measure of the influencing factors under reaction conditions.

It would appear, therefore, that in an interpretation of the relative roles of the factors influencing a series of reactions that $\delta\Delta F$ should be used most commonly to interpret the trends caused by characteristics of the molecules, e.g. inductive and steric effects, whereas $\delta\Delta H$ should be used to correlate the trends due to the molecules' surroundings, e.g. solvation and favoured orientation of the molecules in a particular solvent.

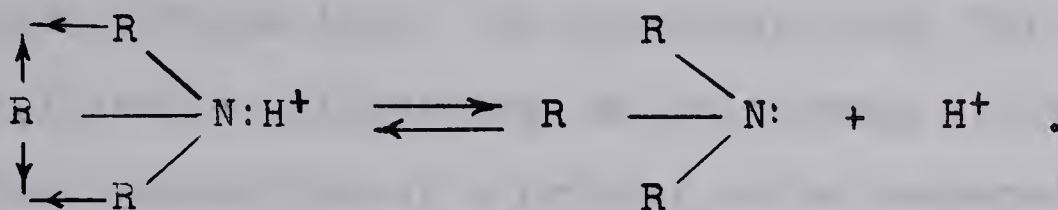
It may be difficult to differentiate between two or more factors influencing a reaction. Consider, for example, the series of methyl amines and ethyl amines, i.e. primary, secondary and tertiary, being protonated. Using the values reported by Bell (56) as tabulated in Table 4, it is apparent that the base strengths are in the order primary $<$ secondary $>$ tertiary and methyl $<$ ethyl. As a first approximation, it would have been expected that on the basis of inductive effects that primary $<$ secondary $<$ tertiary since alkyl groups are more electron donating than protons (59). It has been proposed by H.C. Brown and co-workers that the reversal in the

TABLE 4.

THERMODYNAMIC DATA FOR THE PROTONATION OF AMINES.

AMINE	$-\Delta F$	$-\Delta H$	ΔS	ΔC_p
	kilocalories/mole		e.u.	
ammonia	12.61	12.40	0.7	0
methylamine	14.48	13.09	4.6	-8
dimethylamine	14.72	11.88	9.5	-20
trimethylamine	13.38	8.83	15.2	-41
ethylamine	14.52	13.58	3.5	-
diethylamine	15.00	12.77	7.4	-
triethylamine	14.83	12.21	8.7	-

trend is due to "F" strain and "B" strain (50). "F" strain is concerned with steric interference with the incoming group, so that when an amine is being protonated "F" strain should not be important. "B" strain, on the other hand, may be important due to crowding of the three alkyl groups in a tertiary amine, i.e.



more strained

less strained

It would seem, then, that since ethyl is a larger group than methyl, that "B" should be greater in triethylamine than in trimethylamine. The observed results are diametrically opposed to what would be expected, i.e. ΔF between dimethylamine and trimethylamine is much greater than ΔF between diethylamine and triethylamine. The enthalpy differences are even more in conflict with the "B" strain hypothesis as is shown in Table 4.

Forman and Hume determined the heat of protonation of a series of amines in acetonitrile (50). They found that $-\Delta H$ values for the protonation of ammonia, trimethylamine, triethylamine, tri-*n*-butylamine and tri-*i*-butylamine were 25.0, 24.8, 25.2, 23.9 and 18.1 kilocalories per mole, respectively. One is tempted to speculate from these data that only tertiary amines higher than propyl and particularly those which have branched alkyl chains will exhibit significant "B" strain effects, i.e. the contribution of "B" strain is offset

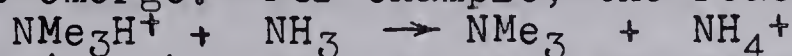
by the increasing inductive effect up to about tri-n-propyl-amine. It would appear, then, that the "B" strain hypothesis cannot account for the differences illustrated in Table 4.

Hall has shown from the stability constants reported in the literature that for a series of amines, the main factor influencing the stability of the protonated species is due to solvation effects (61). On the other hand, Taft (62) has rationalized the differences as an entropy effect, i.e. that upon the protonation of a primary amine compared with a tertiary amine, there will be a greater loss of entropy because there are more protons on the primary amine cation to hydrogen bond with the solvent.

Bell (63) has stated that:

"There is much support for the view (64) that for an ion of moderate size the inner coordination sphere is surrounded by a region which is less ordered than pure water (because of the competition between two incompatible structures), the ordered structure of water returning at still greater distances. The balance between the ordering and disordering effects will determine the entropy of an ion, and in this way a plausible explanation can be given for many observed facts. Since the structure of water is still imperfectly understood, the explanation is essentially a qualitative one, and the position is further complicated by the fact that many nonpolar molecules (for example, the rare gases and the hydrocarbons) have large negative entropies of solution in water, i.e. they increase the order of the solvent (64, 65, 66, 67). Some authors have interpreted this effect in terms of definite cavity structures, such as are found in the solid clathrate hydrates of many gases (68), and others regard it as a "freezing" of the normal water structure.

The above considerations have been applied mainly to ions and molecules which are spherical, or nearly so, and it is obvious that the problem will be much more difficult for unsymmetrical acid-base species.... A few individual explanations do emerge. For example, the reaction



has $\Delta S = -14.5$ (e.u.), and this can be attributed to the shielding action of the methyl groups, which hinder solvent orientation in the ion NMe_3H^+ and hence give it a higher

entropy than NH_4^+ . The same effect appears for a number of amines and has variously been described as hydrogen bonding by the H-atoms of the cation (69) or as solvent exclusion by the alkyl groups (70), the two being equivalent. Unfortunately, however, the specific heat changes are in the opposite direction (for example, $\Delta C_p = 41$ (cal./mole/degree) for $\text{NMe}_3\text{H}^+ + \text{NH}_3 \rightarrow \text{NMe}_3 + \text{NH}_4^+$), and this is certainly unexpected, although explanations can be devised in terms of restricted rotation."

In the above explanation it seems that the tacit assumption is made that the unprotonated species play a minimal role in determining the thermodynamics of the reaction. Suppose, however, that the trimethylamine molecule is surrounded by a solvent cage (or that it promotes "freezing" of the normal water structure) i.e. it is a "structure" maker relative to ammonia, then ΔS would be expected to be a large negative value since the system would be less random in the final state. If this was indeed the case then ΔC_p would be expected to be a large positive value since at lower temperatures (than 25°C) formation of cages about the trimethylamine molecule would be enhanced as the liquid water assumed a more "ice-like" structure; on the other hand at higher temperatures the solvation of ammonia and trimethylamine would tend to become more similar as thermal agitation would diminish the probability of cage formation by the solvent molecules.

The latter argument is in agreement with the findings of H.S. Frank and co-workers (5, 64). It is not clear, however, whether the differences discussed above are due to "iceberg" formation or clathrate cage formation around the unprotonated amine. In the case of tertiary amines in the

series trimethyl, triethyl, and tri-n-propyl there is some evidence in favour of the clathrate cage hypothesis. Whereas trimethylamine is very soluble, triethylamine is soluble to the extent of 15g./l. at 20° and 19.7 g./l. at 65° (71), and tri-n-propylamine is virtually insoluble at room temperature. The solubility data conforms with a clathrate cage hypothesis, i.e. tri-n-propylamine is too large to fit into a cage that would have a reasonable probability of formation which would account for its low solubility in water, whereas the smaller molecules fit into the cavity formed by a dodecahedron. In addition, Pickering (72) has found that trimethylamine and triethylamine form solid hydrates which conform with a clathrate cage hypothesis, i.e. he has reported Me_3N hydrates containing 2, 7, 11, and 20 water molecules per Me_3N and Et_3N hydrates containing 2 and 8 water molecules per Et_3N . It can be argued that these occur at low temperatures, but recent work has shown that some of the ice-like characteristics of water are retained at room temperature (73).

The first part of this project was to develop a calorimeter which could be conveniently used by one experimentalist, to obtain reasonably precise enthalpy data.

The second part of this project was to determine the heats of protonation of a series of monoamines, diamines, and amino acids, and with the enthalpy data determined, in conjunction with stability constants reported in the literature, attempt to elucidate the factors influencing the protonation of these compounds. With the protonation data, an attempt

will be made to explain certain coordination data found for these compounds as ligands complexing with metal ions.

II. THE CALORIMETER

A. Introduction.

Numerous calorimeter designs have been described in the literature, many of which would have been suitable for measuring the enthalpies considered in this thesis. Unfortunately, those that satisfied the required precision were of such a design that their manipulation would be rather inconvenient. The objective of this portion of the research was to develop a calorimeter which could be used conveniently by one experimentalist and which would have a precision of about 1% (95% confidence). A series of calorimeters was built and evaluated against these criteria.

B. Development of the calorimeter.

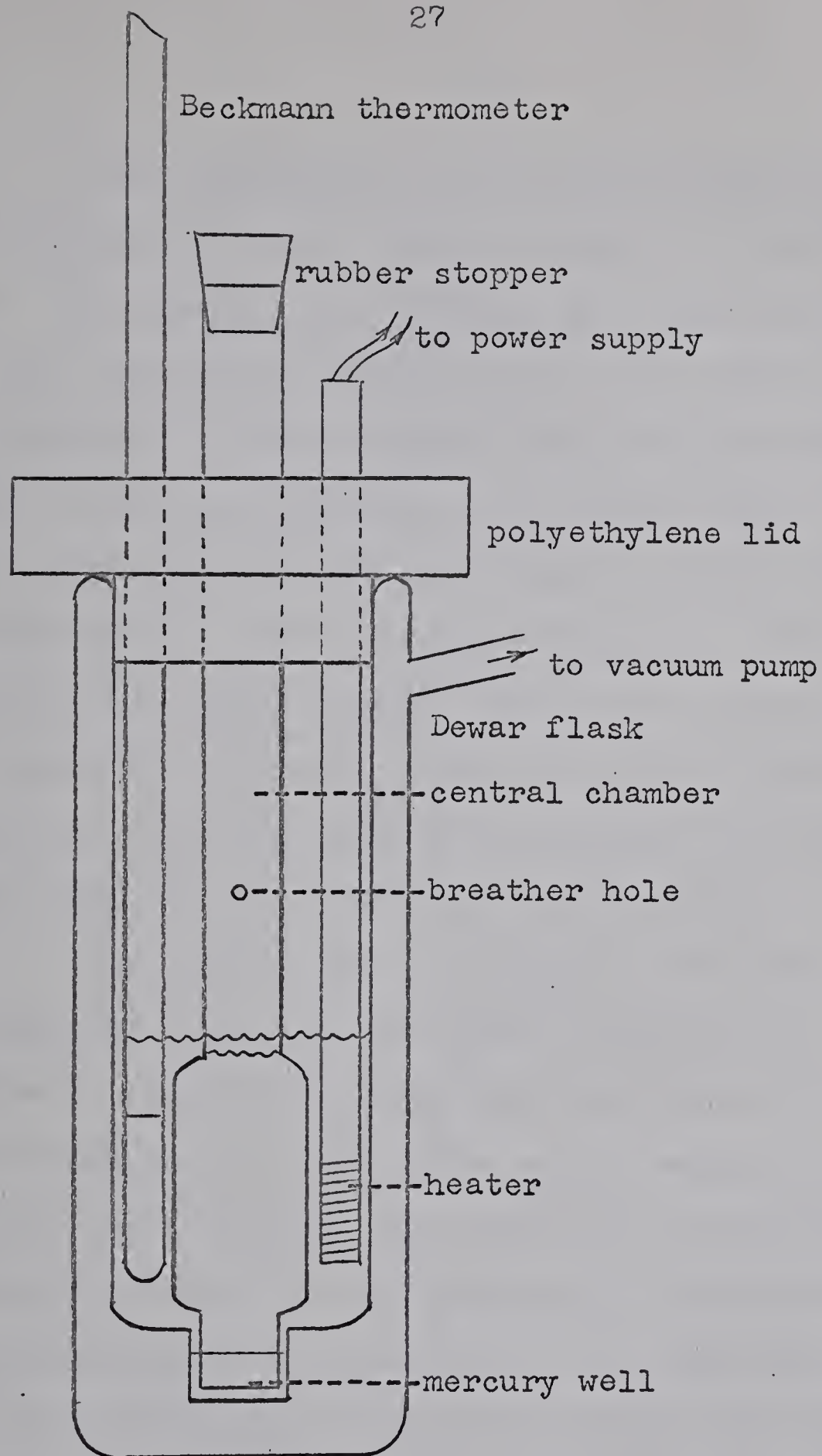
It was decided to use electrical calibration because it provides the most accurate calibration (43) because it allows calibration after each chemical run and thus effectively eliminates any errors due to variations of the heat of stirring, heat capacity of the calorimeter contents and the surroundings from run to run. The temperature of the reactants must be identical or accurately known before the reaction takes place. This can be accomplished in various ways, e.g. the reactants can be separated in the calorimeter by removable plugs (31, 41), mercury locks (74, 75), ampoules which are crushed (76) introduction pipets (77) or thermostated burets (78).

1. Calorimeter Mark I. Figure 2.

The simple calorimeter described by Brown and Horowitz (75) satisfied these conditions. The reactants were separated by a mercury well and the heat capacity was calibrated electrically. Such a calorimeter was constructed and tested using the reaction:



The details of the assembled calorimeter are shown in Figure 2. The heater was a thirty inch length of twenty-six gauge manganin wire which was wound on a threaded one half inch O.D. Teflon tube which was mounted through the lid. The heater leads were eighteen gauge copper wire which lead out through the Teflon tube to lead storage batteries which acted as the potential source. The heater was provided with an electrically insulating coating of polyurethane plastic (Plastiglo Industries, Limited). This coating was applied by repeated dipping in the monomer and allowing polymerization to occur in situ. The central chamber was an all glass structure which could be raised and lowered to allow mixing of the two reactants and to provide stirring. The Dewar flask as shown in Figure 2 was constructed such that it had a mercury well and such that it could be evacuated at will. The calorimeter lid was machined from high density polyethylene. It fitted tightly into the Dewar flask and had three holes drilled in it for the thermometer, the central chamber, and the teflon heater form. The temperature sensing device was a Beckmann thermometer.



$\frac{1}{2}$ full scale

Figure 2 . Calorimeter Mark I.

The calorimeter was assembled and placed in the constant temperature bath. Enough mercury to fill the well was added. One reactant was pipetted into the outer chamber and the other reactant was pipetted into the inner chamber. After the temperature of the contents was the same as the bath temperature, vacuum was applied to the Dewar flask. The temperature was read and recorded at 30 second intervals for a 10 minute fore-period. At zero time, the mercury seal was broken by raising the inner chamber. The inner chamber was raised and lowered in a regular fashion to provide stirring. Simultaneously, the temperature was read and recorded at 30 second intervals for a 15 minute after-period.

The calorimeter was cooled to the bath temperature; releasing the vacuum in the Dewar decreased the time required for this to occur. The calibration was done by passing direct current through the heater immersed in reaction mixture. The electrical heat released was determined by measuring the potential drop across a known resistance in series with the heater whose resistance was known for a measured period of time. The temperature, potential and the time were read and recorded simultaneously. While these operations were being performed, the calorimeter contents were stirred with the inner chamber.

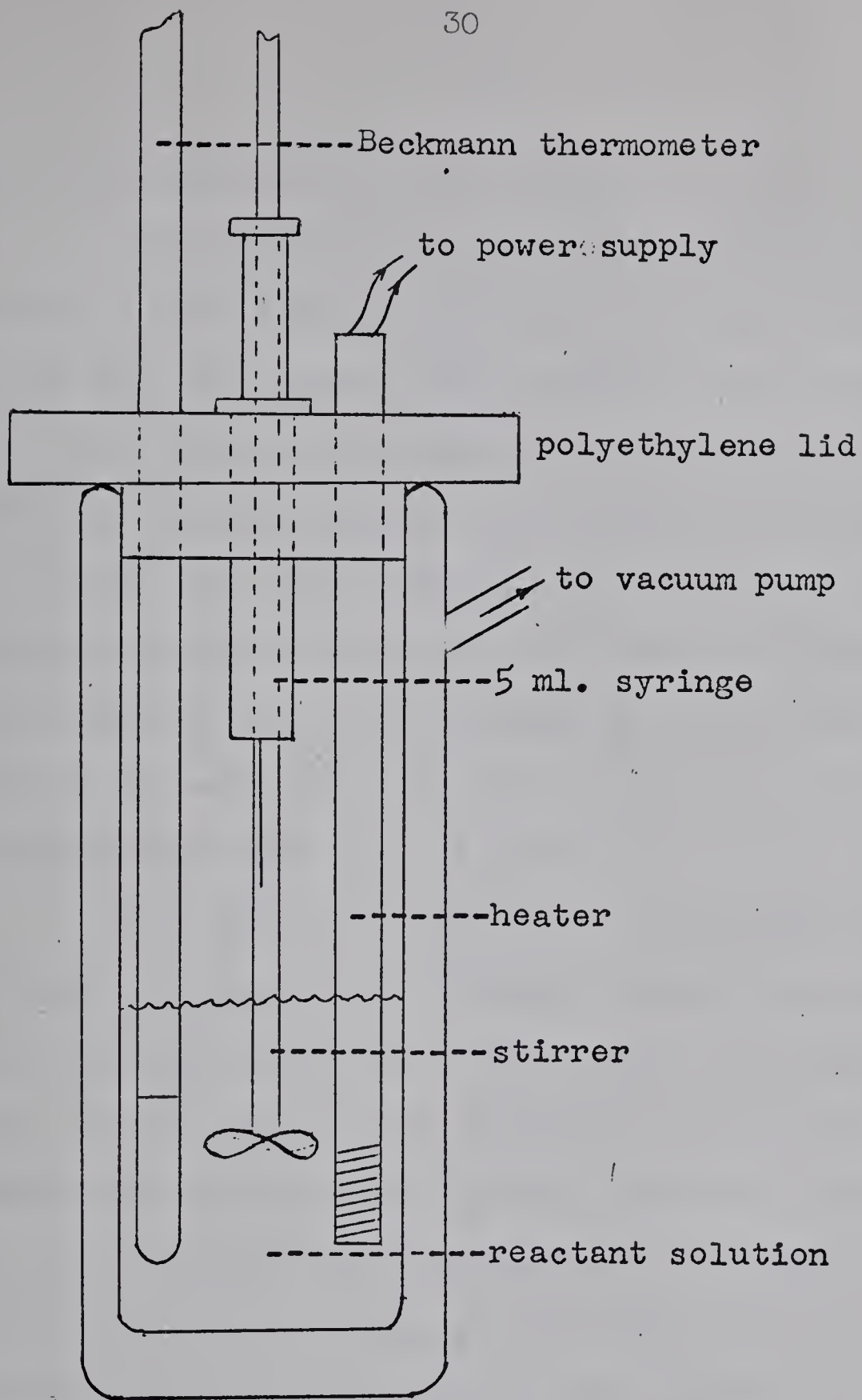
A series of runs was performed using the reaction of sodium hydroxide and hydrochloric acid it was found that the probable deviation of a single determination was 0.74%. This corresponds to 95% confidence limits of 2.2% which is

not satisfactory. Part of the lack of precision was undoubtedly due to inexperience of the operator, but part was due to the number of operations which had to be done simultaneously. That is, the solution was stirred, the thermometer was read, the potentiometer was balanced, the heater was switched on and off, and the temperature, time and potential were recorded. To perform all of these operations caused undue inconvenience of operation for a single experimentalist.

2. Calorimeter Mark II. Figure 3.

It was decided to use a motor driven stirrer. This would provide better stirring of the calorimeter contents. The Mark I was not adaptable to a motor driven stirrer so instead of the mercury well structure, it was decided to use a syringe for one of the reactants. The motor driven stirrer was mounted through the center of the calorimeter lid by means of two steel roller bearings.

The calorimeter was assembled and one reactant was added to the calorimeter by pipetting it through the syringe hole. A 5 ml. syringe was filled with the other reactant and capped with a weighed serum cap. The full syringe was weighed and fitted into the syringe hole in the calorimeter lid. After allowing the temperature of the syringe and the calorimeter contents to equilibrate, (by leaving it in the calorimeter for ~ 30 minutes) the chemical run was begun. At zero time the syringe was quickly emptied, removed and weighed. The calibration was carried out in the same manner as for the Mark I experiments. Not enough runs were done to provide



$\frac{1}{2}$ full scale

Figure 3. Calorimeter Mark II.

data on the precision of this model.

The chemical and electrical heating curves are shown in Figure 4 (the linear fore-period has been deleted). The shape of the two curves differ greatly, which was partly due to the linear addition of heat in the electrical calibration and the low thermal conductivity of the Teflon heater form, which caused the heat produced to be dissipated slowly. It has been recommended by White (43) that the chemical and calibration heating curves be as similar as possible so that errors in the extrapolation to zero time can be minimized.

3. Calorimeter Mark III. Figure 5.

This model was the same as the Mark II, except that the heater was wound on a threaded brass tube which was coated with polyurethane plastic. The heater was supported by two $\frac{1}{2}$ " o.d. Teflon tubes which contained the heater leads. The stirrer blade was situated in the center of the brass heater form. The stirring was improved over the Mark II because the solution was drawn up through the brass tube and down the outside. The electrical heating was considerably improved because the heater was not as localized and the electrical heat was quickly dissipated to the solution as shown by the linearity and small lag of the heating curve illustrated in Figure 5.

The Mark III still had two distinct disadvantages. The number of experimental readings was still too great to be made conveniently by one operator. The length of time for the calorimeter to return to the bath temperature between the

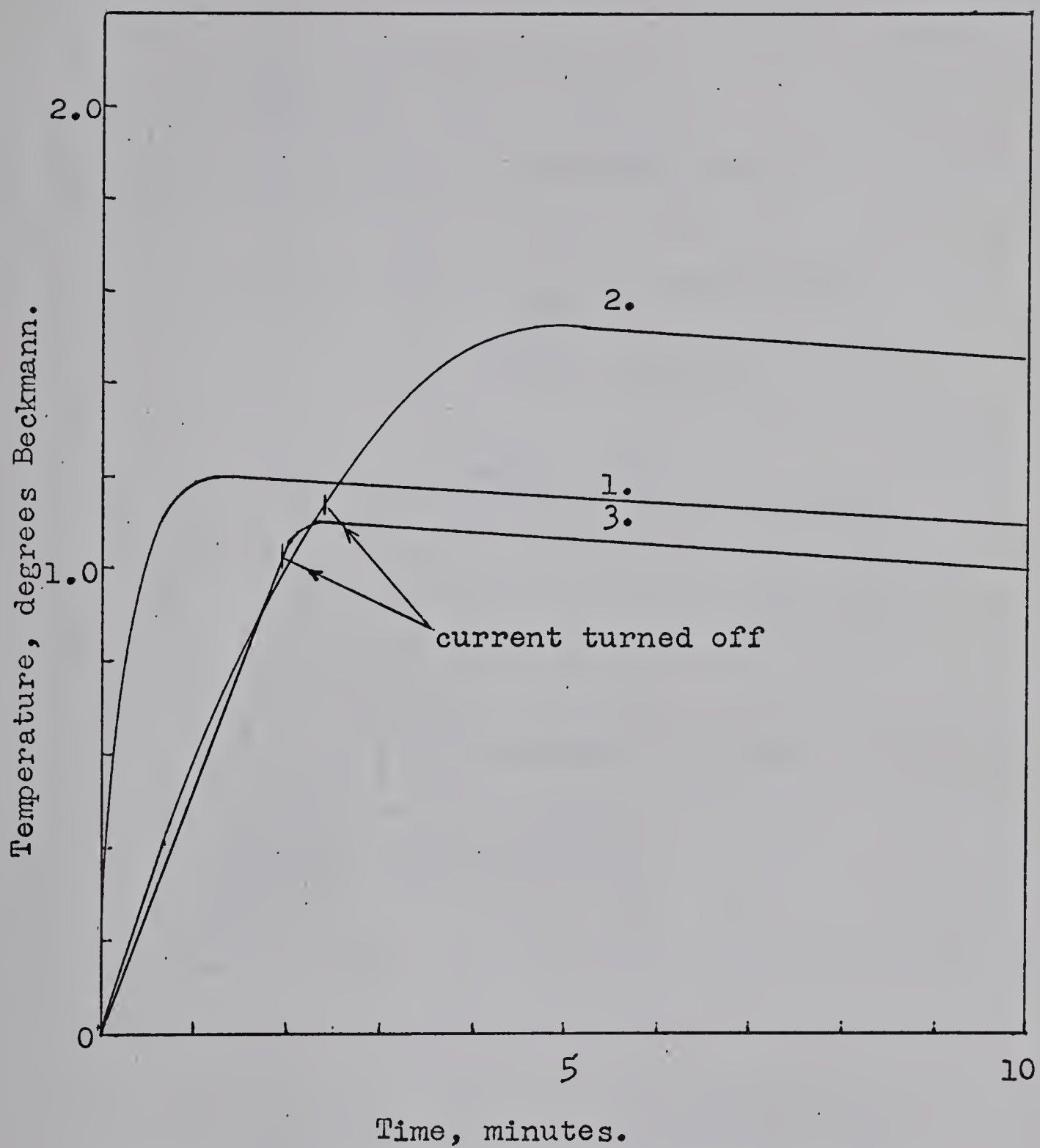
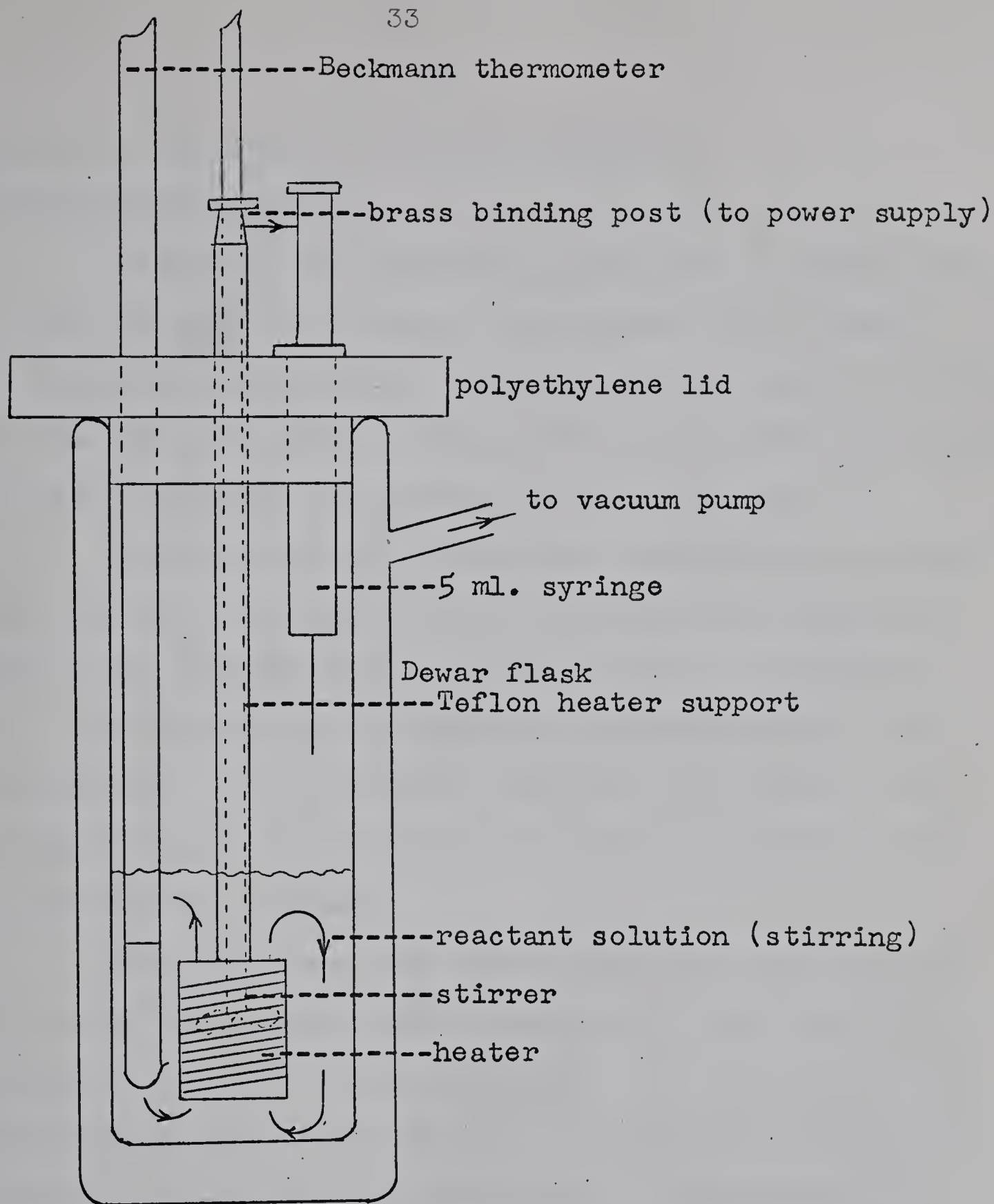


Figure 4. Heating curves from Calorimeter Mark II and Mark III.

1. chemical heating curve.
2. electrical heating curve (Mark II).
3. electrical heating curve (Mark III).



$\frac{1}{2}$ full scale

Figure 5 . Calorimeter Mark III.

chemical and calibration runs was excessive.

4. Calorimeter Mark IV.

This model was identical to the Mark V, except that a syringe was used to introduce the reactant (HCl) rather than the motor driven buret. The detailed description will be deferred until the next section. The reaction of hydrochloric acid with sodium hydroxide was used to evaluate the Mark IV.

A solution of $\text{HCl} \cdot 10 \text{H}_2\text{O}$ was prepared by diluting a weighed amount of concentrated hydrochloric acid (Baker and Adamson reagent grade) with a weighed amount of distilled water. The solution was standardized gravimetrically with silver nitrate, i.e. a weighed amount of the solution was added to an excess of silver nitrate and the resulting silver chloride was weighed.

Some carbonate free sodium hydroxide solution was added to the calorimeter from a pipet, such that there was an excess of about 5% sodium hydroxide. The solution in the calorimeter was diluted to 250 ml. by pipetting freshly boiled distilled water into the calorimeter. The hydrochloric acid was added as previously described (see Mark II).

The result of the similar series of calorimetric runs using the Mark IV are reported in Table 5. It can be seen from the results that the heats of neutralization found were consistently less exothermic than those reported by Richards and Rowe (79). This was due to evaporation of residual acid before a weighing of the empty syringe could be made. The apparent amount of acid used was, therefore,

TABLE 5.

THE HEAT OF NEUTRALIZATION OF SODIUM HYDROXIDE WITH HYDRO-
CHLORIC ACID USING A SYRINGE TYPE CALORIMETER, AT 20° CENTIGRADE.

Run	Molality (NaCl formed)	ΔH , Richards - Calories	ΔH , Found - Calories	% Deviation
1 A	0.067	13,758	13,663	-0.69
2 A	0.067	13,758	13,685	-0.53
4 A	0.050	13,737	13,673	-0.47
5 A	0.050	13,737	13,693	-0.32
1 B	0.098	13,792	13,685	-0.78
2 B	0.098	13,792	13,620	-1.25
3 B	0.098	13,792	13,653	-1.01
4 B	0.079	13,772	13,725	-0.34
5 B	0.079	13,772	13,754	-0.13
6 B	0.079	13,772	13,771	-0.01
7 B	0.059	13,748	13,770	0.16
8 B	0.059	13,748	13,628	-0.87
9 B	0.059	13,748	13,706	-0.31
10 B	0.059	13,748	13,681	-0.49

greater than the amount of acid actually taking part in the calorimetric determination. The results were on the average 0.5% low; but the relative 95% confidence limits were found to be less than 1%. Because of the negative bias further refinements were made.

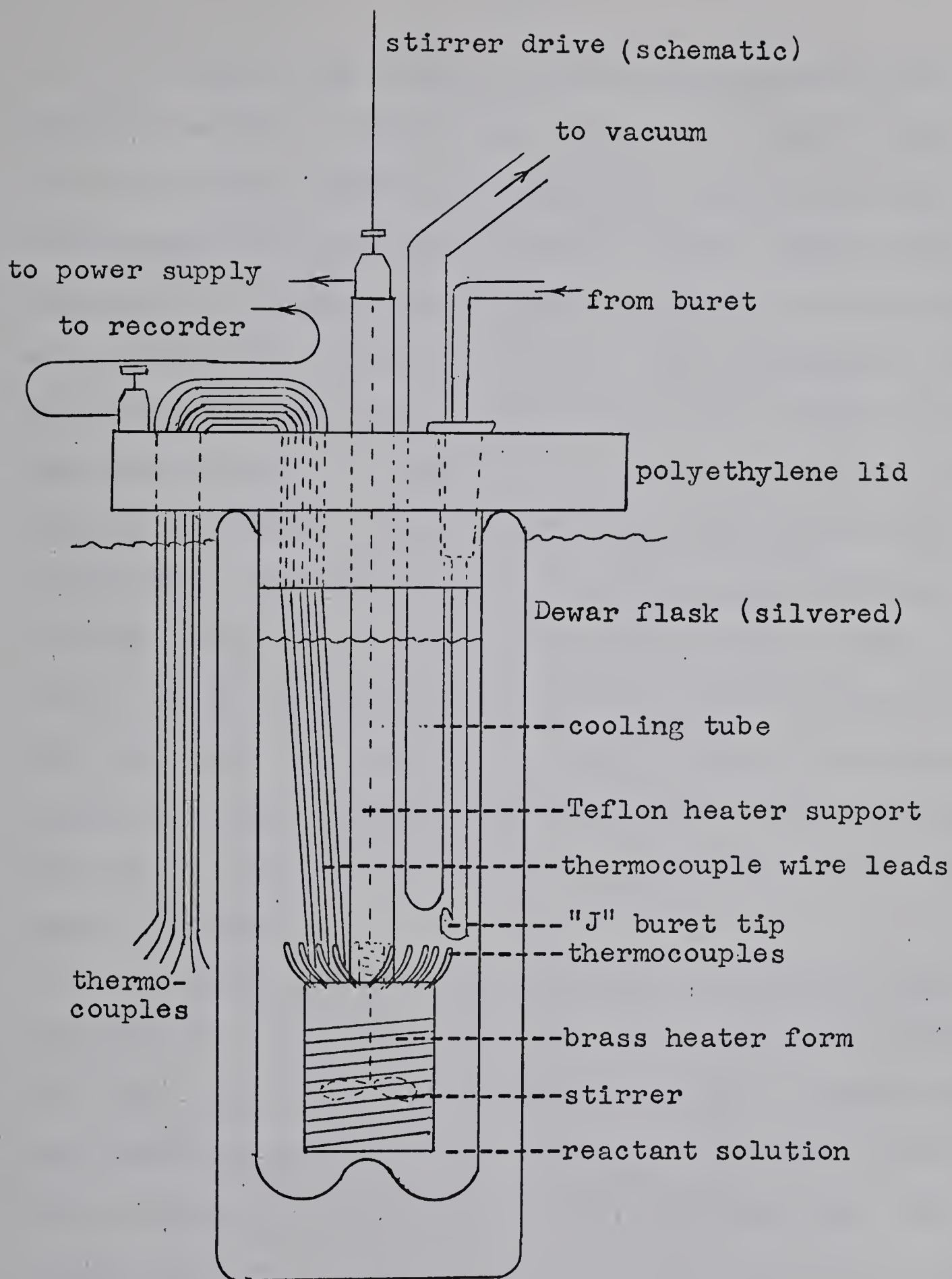
5. Calorimeter Mark V.

This calorimeter proved to combine the required sensitivity and the desired convenience of use. The Mark V basically consisted of a Dewar flask, thermocouples in conjunction with a recording potentiometer, a motor driven buret and an electrical calibration heater (see Figure 6 and 11). A complete description of the calorimeter used for determining the heats of protonation reported in this thesis follows.

a. The temperature sensing device.

It was decided to use a temperature sensing device whose signal could be readily and continuously taken out on a recording potentiometer. In this way the complete time-temperature curve would be available. The experimentalist would be free to devote his attention to the remaining details of calorimeter operation. In addition, the intimate details of the temperature profile were more clearly defined. The temperature lag, the point of complete reaction, and in the case of two groups being protonated, the onset of the second protonation, were all specifically detailed.

The three devices which could readily be adapted to a recorder are a resistance thermometer, a thermistor, or a thermocouple. Thermocouples require no auxiliary electrical circuitry and a standard temperature sink is readily available by using the constant temperature bath. Even though a higher sensitivity is more easily attained with a resistance thermometer or thermistors, the use of thermocouples provided the simplest temperature sensing device available.



$\frac{1}{2}$ full scale

Figure 6 . Calorimeter Mark V. An internal view of the reaction flask when assembled.

Thirty-two iron-constantan thermocouples were connected in series in such a way that sixteen were in the calorimeter and sixteen were in the constant temperature bath. The thermocouple wire used was 20 gauge, Teflon coated, type J (Honeywell). It had poor abrasion resistance so each length was covered with a polyvinyl sleeve. The calorimeter couples were mounted on the heater form (Figure 6.) by passing each wire through one of a series of 0.1" holes situated symmetrically in two rows on the perimeter near the top of the brass heater form. The bottom row of holes was used for the iron wires and the top row for the constantan wires. Every second couple was in the calorimeter pointing out from the heater form, and they were connected to the couples in the bath by passing each wire through a $\frac{1}{2}$ " hole in the calorimeter lid over the lid and through another hole into the bath as illustrated in Figure 6.

After all the iron-constantan connections had been made, the two ends were soldered to two copper wire leads such that these connections would be in the constant temperature bath during a run. The leads were soldered to two brass binding posts mounted on the calorimeter lid. The thermocouples were welded by burning the tips with a small flame from a glass-blowing torch. The entire thermopile assembly was coated with several coats of polyurethane plastic by successive dipping and a painting procedure.

The thermopile was connected to a Sargent model SR recording potentiometer through the binding posts on the lid.

A shielded cable was used between the thermopile and the recorder.

The full scale deflection of the recorder was 1 millivolt. The deflection produced by a 1° centigrade difference between the calorimeter contents and the bath was found to be 206.2 divisions (full scale deflection was 250 divisions). Full scale deflection was, therefore, 1.212° centigrade. The sensitivity was 0.1 divisions or 0.0005° centigrade. The temperature response of the thermopile was found to be linear between 20° and 30° centigrade within experimental error.

b. The calibration heater. Figure 6.

The heater was a twenty foot length of manganin wire which had a nominal resistance of 5 ohms per foot. The silk covered wire was wound on a finely threaded 4.5 cm. diameter brass tube which had been coated with polyurethane plastic. Two $\frac{1}{2}$ " o.d. Teflon tubes were attached by threaded brass studs to the heater form. The heater leads were 18 gauge copper wire soldered to the ends of the manganin wire. Each lead passed through a hole drilled in one of the brass studs and into one of the Teflon tubes to a brass binding post located on the lid. The heater assembly was held in place by the Teflon tubes which fitted tightly into holes drilled in the calorimeter lid. The whole assembly was covered with several coats of polyurethane plastic.

The resistance of the heater was found by using a Wheatstone bridge which could be used to determine resistances to five significant figures. The method used was to

alternately measure the resistance of the heater and a Rubicon Instruments N.B.S. type 100 ohm standard resistor (model 1102). The standard resistor had a calibrated resistance of $100.00\bar{1}$ ohms and it had guaranteed error limits of less than 0.01% for wattage dissipations up to 0.1 watt. The resistance of each was determined at a series of resistance arm ratios. The data is listed in Table 6. The median resistance of the heater was found to be 98.525 ohms and the probable deviation was 0.003 ohms.

c. The stirrer. Figure 7.

The stirrer consisted of a $\frac{1}{4}$ " diameter brass rod attached by a screw to a $1\frac{1}{4}$ " propellor-shaped brass blade. The drive rod passed through a steel roller bearing and was attached to a $\frac{1}{4}$ " diameter Teflon rod by a $1\frac{1}{4}$ " length of $\frac{1}{2}$ " x $\frac{1}{4}$ " Teflon tube with shear pins. The Teflon rod passed through another bearing and was connected to another brass rod by a 5" length of Teflon tube. The parts in the calorimeter were covered with several coats of polyurethane plastic.

The Teflon rod acted as a thermal insulator so that the heat leakage between the calorimeter contents and the surroundings was minimized. The steel bearings fitted tightly in a hole drilled in the center of the calorimeter lid. The blade of the stirrer was then situated in the center of the heater-thermopile form so that the stirring was enhanced by forcing the solution up through the tube.

The stirrer was driven at about 200 R.P.M. by an electronically controlled variable speed motor (Gerald K. Heller, model GT21). The stirring was found to be efficient,

TABLE 6.

DETERMINATION OF THE RESISTANCE OF THE CALIBRATION HEATER.

Ratio	Standard	Heater	Heater Resistance (R_H) (Calculated)	δR
1:1	99.80	98.31	98.507 ohms	-0.018
2:1	199.56	196.62	98.527 ohms	0.002
3:1	299.33	294.90	98.520 ohms	-0.005
4:1	399.08	393.18	98.522 ohms	-0.003
5:1	498.83	491.48	98.527 ohms	0.002
6:1	598.60	589.80	98.530 ohms	0.005
7:1	698.42	688.12	98.525 ohms	0.000
8:1	798.20	786.45	98.528 ohms	0.003
9:1	897.99	884.73	98.523 ohms	-0.002

$$R_H = \frac{100.001 \times \text{Heater}}{\text{Standard}}$$

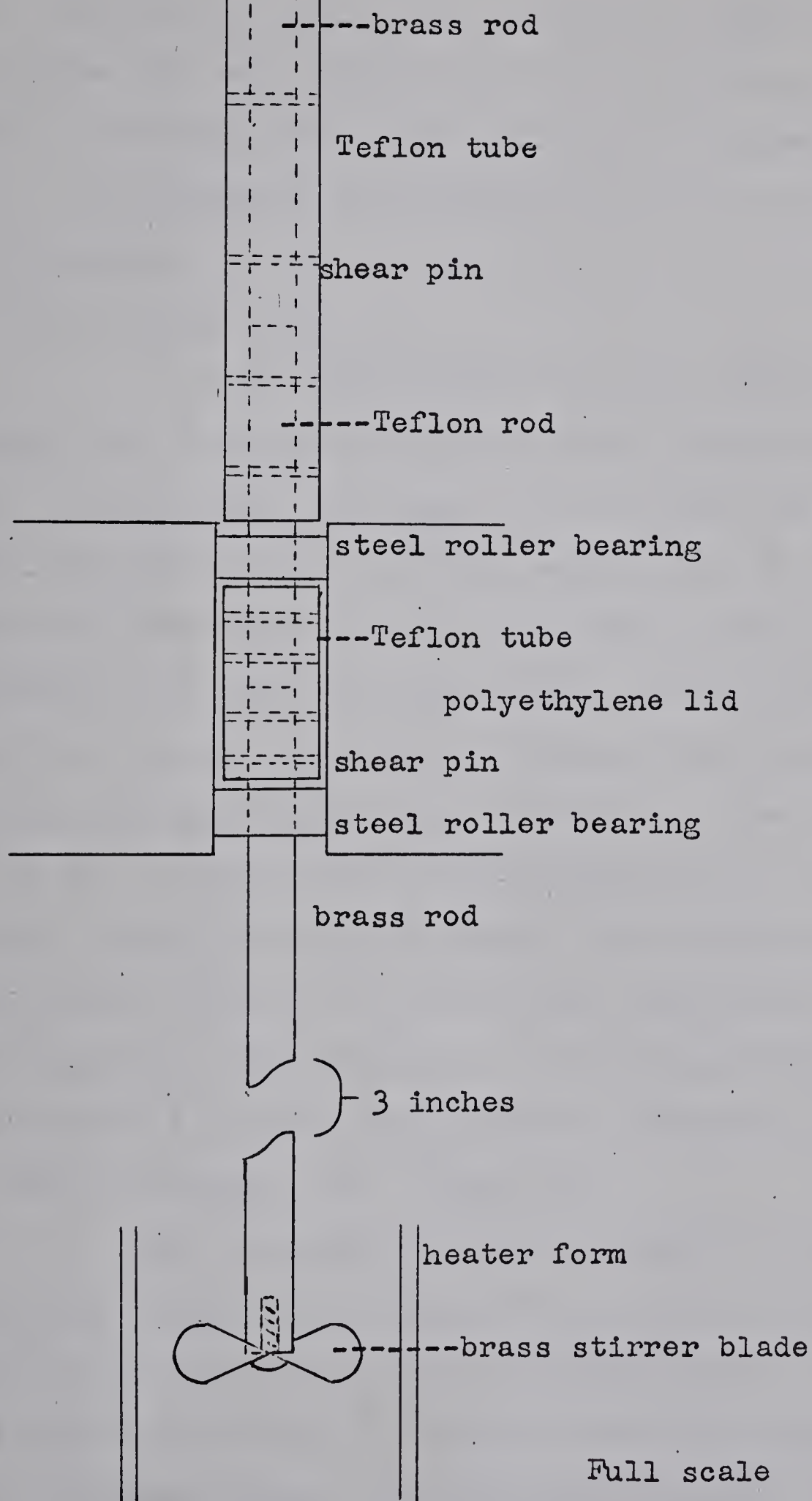


Figure 7. Stirrer assembly.

i.e. there was no lag in the temperature response due to stirring when heat was produced in the calorimeter. There was heat of stirring, but it was constant throughout an individual run, as indicated by the linearity of both the fore-period and after-period.

d. The cooling tube.

A cooling tube similar to that used by Davies, Singer, and Staveley (31) was inserted through the calorimeter lid. It was a six inch long, $\frac{1}{2}$ " o.d. glass tube, sealed at the lower end and with a 10/30 female joint at the upper end. When the temperature of the calorimeter contents was to be decreased, the tube was filled with the appropriate amount of powdered dry ice (estimated). A male joint leading to a vacuum pump was inserted and the tube was evacuated. By using the cooling tube in conjunction with the calibration heater, it was possible to adjust the temperature of the calorimeter contents to the desired temperature in less than five minutes. The position of the cooling tube in the calorimeter is schematically shown in Figure 6.

e. The calorimeter lid. Figure 8.

The calorimeter lid was machined on a metal working lathe using a slow speed, from high density polyethylene. The top part of the lid was 0.9" thick and 6" in diameter and the bottom part was 0.9" thick and was machined to fit tightly into the Dewar flask. Six holes were drilled through the thickest part. Four $\frac{1}{2}$ " holes were used for the entry of the thermocouple leads, the cooling tube, and the two Teflon

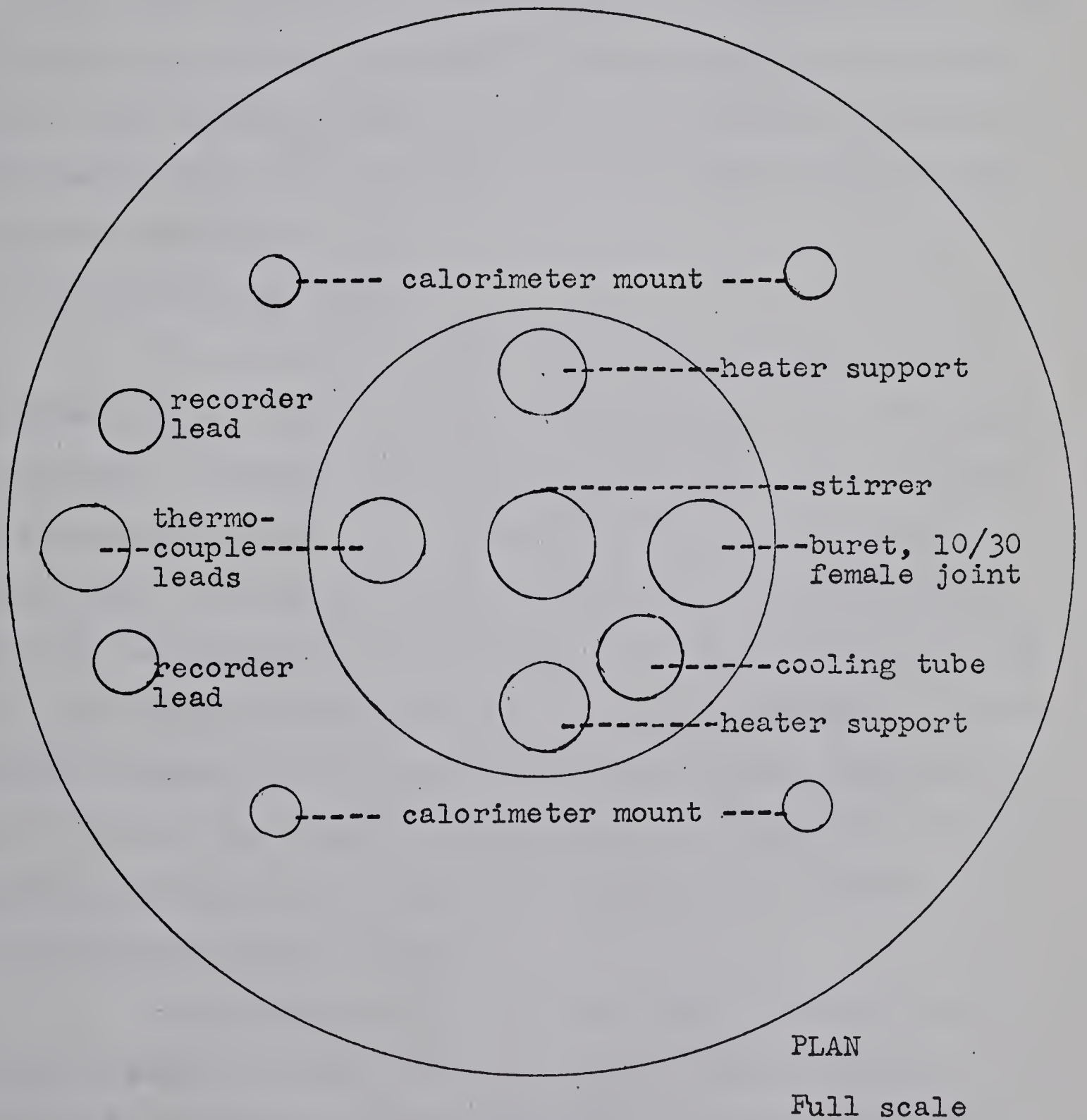
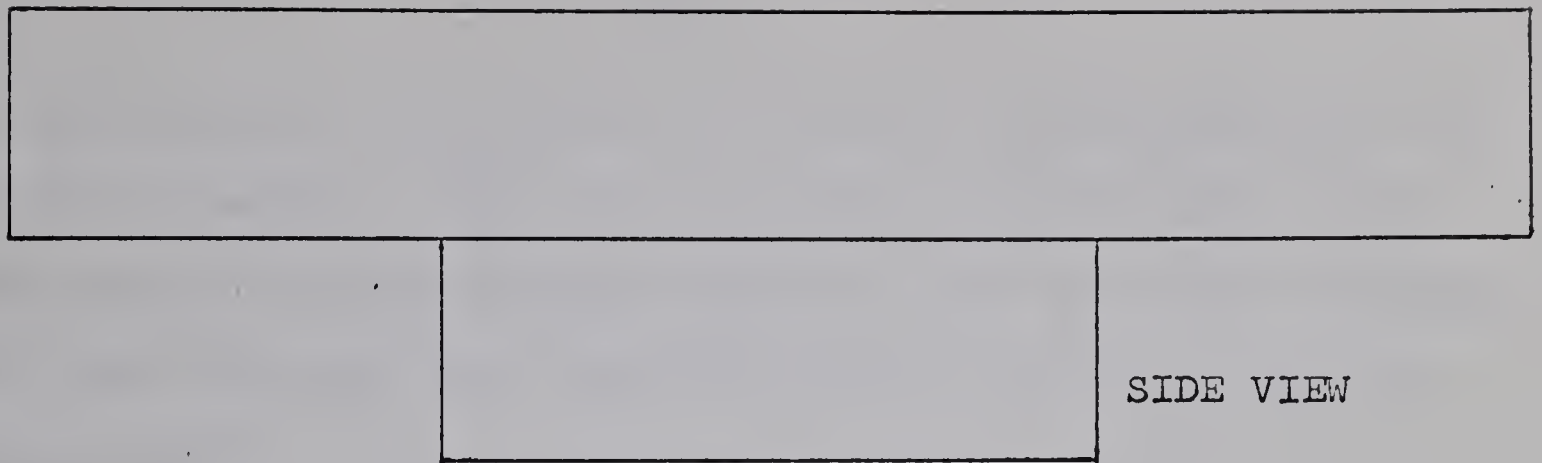


Figure 8 . Calorimeter lid.

heater supports. A $\frac{5}{8}$ " hole was drilled in the center for the stirrer assembly. A $\frac{9}{16}$ " hole in which a 10/30 female joint was sealed with epoxy cement served as the entry for the buret tip (this hole was also used for the syringe in the Mark IV experiments).

Seven holes were drilled through the lid lip. Four $\frac{1}{4}$ " holes were used for the rods of the calorimeter mount. Two $\frac{3}{8}$ " holes were drilled in which the brass binding posts from ends of the thermopile were mounted. A $\frac{1}{2}$ " hole was used for the thermocouple leads between the calorimeter core and the standard temperature sink.

f. The calorimeter mount.

The calorimeter mount consisted of a 4" square aluminum plate, covered with a rubber gasket. Four 13" long, $\frac{1}{4}$ " diameter, threaded brass rods were mounted at the corners of the aluminum plate, i.e. they were fixed in place with steel nuts. 12 inches of each rod extended above the plate. When the components were assembled as shown in Figure 11, the rods were fitted through the holes in the calorimeter lid and tightened down with wing nuts. The calorimeter mount sat on the bottom of the constant temperature bath during a run and served to stabilize the apparatus (minimized vibration).

g. The Dewar flask. Figure 6.

Since the cooling tube was added to the design, it was possible to use a silvered Dewar flask. This decreased the thermal leakage very significantly. The Dewar flask which was 9" high, whose o.d. was 3.6" and whose i.d.

was 2.6", had a capacity of about 760 ml. When the calorimeter core was inserted the capacity was about 512 ml. An indentation in the bottom of the flask enhanced the stirring by eliminating the "dead" volume that normally would be present due to the solution flow around the heater form.

h. The buret assembly. Figure 9.

The buret was a 10 ml. piston driven buret with a digital readout which could be read to 0.0001 ml. (Manostat model 15401 micropipet-buret). It was modified in the following ways. The fiber bearing on the drive shaft was replaced with a steel roller bearing mounted in the counter casing. Thus friction was reduced considerably. Instead of turning the drive by hand, a 2 R.P.M. synchronous motor (Sargent model S72183) was used. The motor was attached to the counter casing as illustrated in Figure 9. The motor drive shaft was connected to the buret drive shaft with an interchangeable set of gears. By changing the gears, flow-rates from 0.04 to 2.5 ml. per minute could be attained. The flow-rate used for all the experimental determinations was 2.5 ml. per minute, i.e. a 96 tooth gear was mounted on the motor drive shaft and a 24 tooth gear was mounted on the buret drive shaft. The motor was connected in parallel with an electrical clock (Precision Scientific model 126893) so that any discrepancies between the time and the volume delivered would be readily apparent, e.g. due to slippage of the motor or skipping of the gears.

The original buret tip was replaced by a three-way

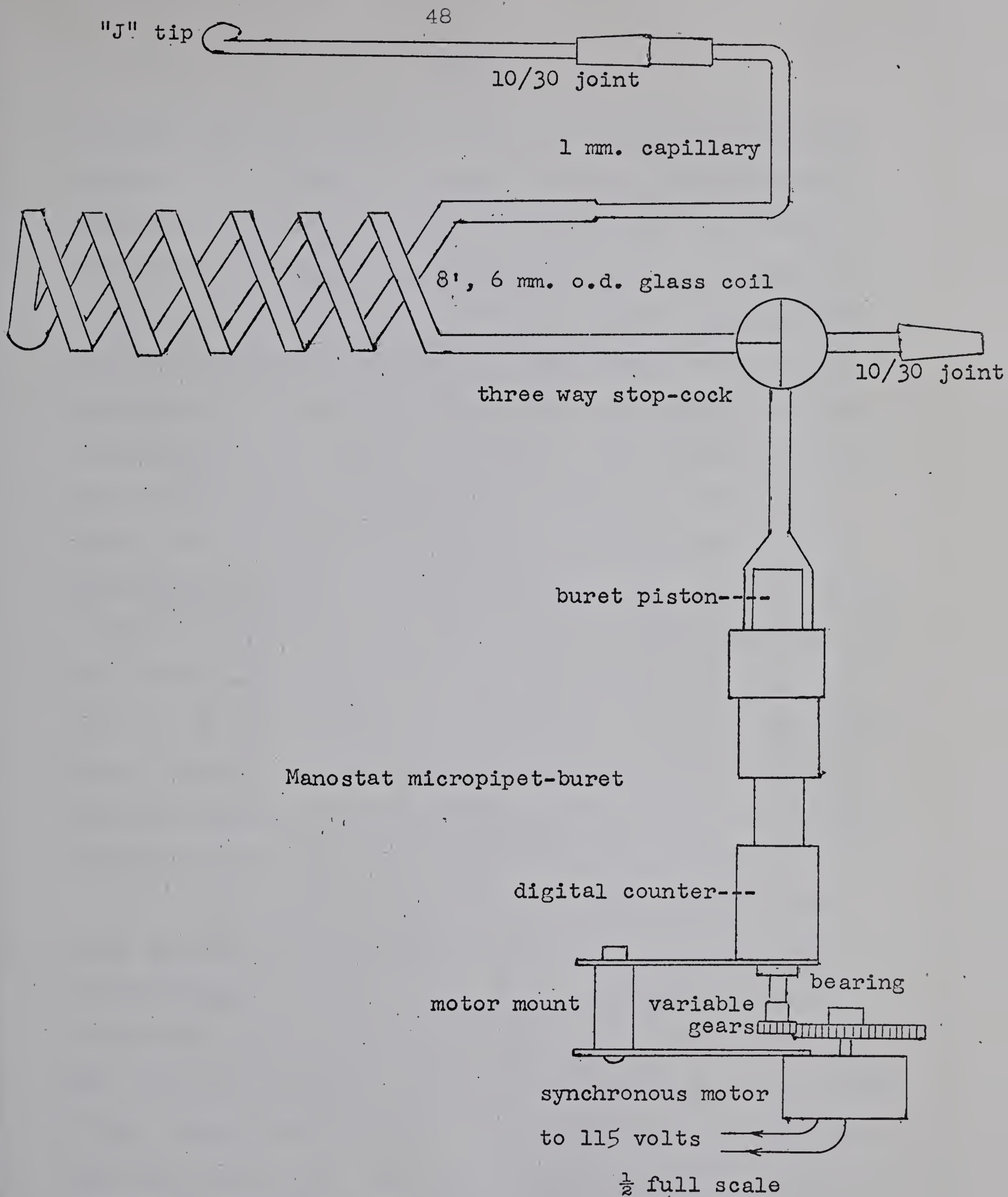


Figure 9 . Buret assembly.

stopcock. One arm led to a 6 mm. o.d. glass coil which was made from an 8' length of tubing, which was connected to a 12" long, 1 mm. bore capillary. A 10/30 male joint which fitted into the calorimeter lid was cemented on to the capillary about 6" from the end. The tip of the capillary was drawn out to about a 0.1 mm. bore and formed into a "J" to minimize diffusion of the titrant into the bulk of the solution before the titration was begun. The effectiveness of the "J" was tested by placing the carefully rinsed tip in 500 ml. of distilled water which was being stirred. After about twenty minutes, the pH was always higher than 5. Since in most calorimetric runs about 5 ml. of 4.9117 molar HCl was used, less than 0.02% of the acid would have diffused into the bulk of the solution in the pre-run. In most cases there was an excess of the reactant being titrated and presumably the same amount of diffusion would occur in the post-run and therefore there would be no error from this source.

The second arm led to the buret cylinder. The third arm led to a 10/30 male joint which fitted into the storage flask of titrant. The storage flask was a 2 liter separatory funnel which had a 10/30 female joint on its outlet. To fill the buret, the buret was connected to the flask by the joints and the buret stopcock was turned so that all three arms were open. The gears were disengaged and the buret was filled by rotating the buret drive by hand. Simultaneously the tip was washed out by allowing some of the titrant to flow through by gravity feed.

i. The electrical components and circuitry. Figure 10.

The source of current for the calibration heater was made up of six lead storage batteries (12 volt) connected in series. The batteries were charged with a battery charger consisting of a variable transformer (Superior Electric, model 7674), an isolation transformer (Hammond, model 171B60), and a silicon half-wave rectifier. The batteries were kept on charge between runs by closing switch A. The power supplied to the heaters was controlled by adjusting the potential divider so that the rate of electrical heating was similar to the rate of chemical heating.

The dummy heater was a 100 ohm knife heater, mounted in a 5 liter glycerol bath to maintain constant temperature. The dummy heater was on throughout the entire calorimetric determinations, except when the calibration heater was on. This provided a steady source of potential which only varied by a few tenths of a millivolt during the actual calibration.

The current supplied to the calibration heater was determined by measuring the potential drop across the standard resistor, R_A , (Rubicon Instruments, model 1100, 1.00000 ohm N.B.S. type) with a potentiometer (Rubicon Instruments, model 2730). The switch C_1 - C_2 was a double pole double throw switch. When it was in the C_1 position, it supplied direct current to the calibration heater and 115 volt a.c. to the electrical timer (Precision Scientific, model 126893) so that the duration of electrical heating was known accurately. When

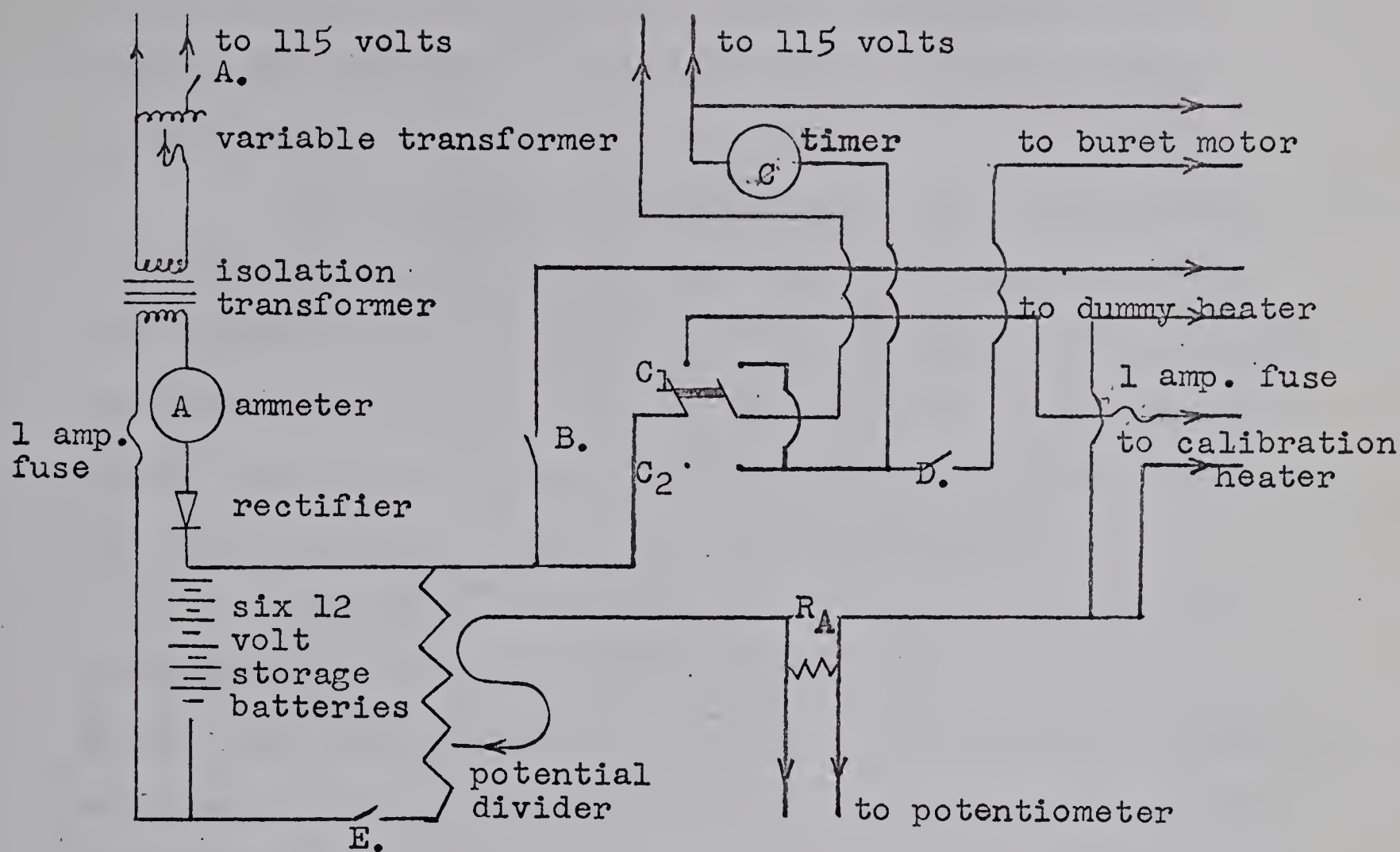


Figure 10. Heater, buret, and timer circuitry.

Components

- variable transformer...Superior Electric, 7674.
- isolation transformer...Hammond, 171B60.
- ammeter...Shurite, 484046.
- timer...Precision Scientific, 126893.
- potentiometer...Rubicon Instruments, 2730.
- buret motor...Sargent, S-72183.
- R_A...Rubicon Instruments, 1100, 1.00000 ohm N.B.S.
type standard resistor.

it was in the C_2 position, and switch D was closed, a.c. current was supplied to the timer and to the buret motor.

j. The constant temperature bath.

The constant temperature bath not only provided constant thermal surroundings for the calorimeter, but was the standard temperature sink for the thermopile and provided the known temperature of one of the reactants, i.e. the coil of the buret was situated in the bath during the calorimetric runs which kept the titrant at a constant temperature.

The bath consisted of a stainless tank which was insulated with 2" of cork and which held about 27.7 liters of water. The temperature was controlled by a Sargent Thermonitor, model S-W, in conjunction with a Sargent Heater and Circulator. The temperature sensing device was a thermistor with a resistance of 2000 ohms at 25°C. The temperature was controlled coarsely by balancing the effects of a stream of air bubbling through the water, which cooled by inducing evaporation and which also enhanced stirring, and the coarse adjustment heater of the Thermonitor. The temperature was finely adjusted with the Thermonitor. A Beckmann thermometer was situated in the bath near the thermopile of the calorimeter which was immersed in the bath. It was found that the temperature of the bath was controlled within 0.0011° centigrade (95% confidence limits) during the calorimetric runs by periodically reading the Beckmann thermometer, which had been calibrated against an N.B.S. calibrated thermometer.

There were no perceptible temperature differences

within the bath, i.e. the differences, if any, were less than 0.001°C . If about 10 ml. of cold water (15°C .) was added to the bath 12" from the thermopile, a temperature change of about 0.003°C was recorded within 6 seconds, or just longer than the response time of the thermopile. This indicated that the stirring of the bath was excellent.

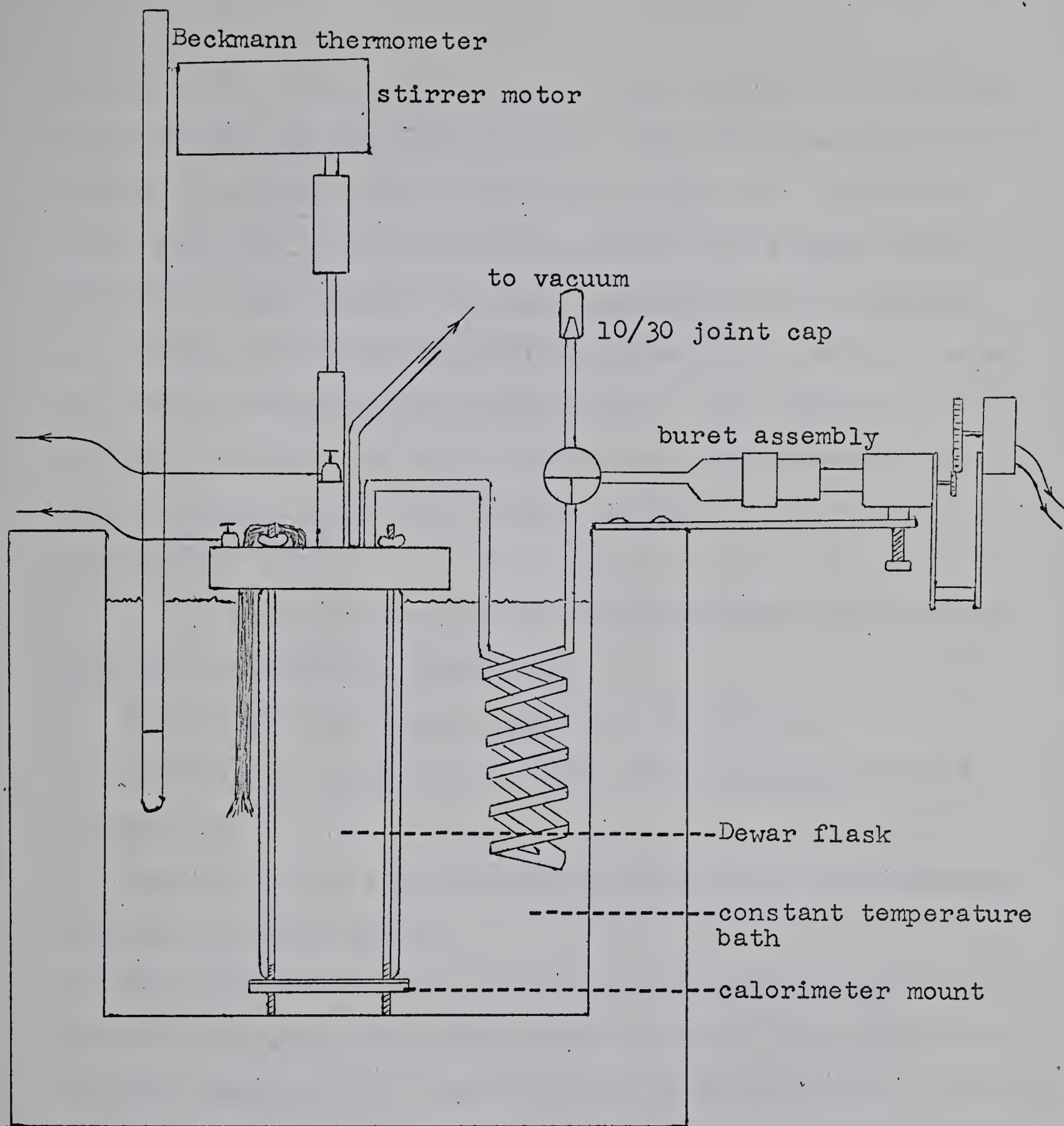
k. The thermostatted room.

All the calorimetric experiments were done in a thermostatted room which was controlled at $25 \pm 0.50^{\circ}\text{centi-}$ grade. In a constant temperature room it was much easier to obtain the necessary control of the constant temperature bath. It also had other important advantages, e.g. the reagents were kept at a constant temperature. This was particularly advantageous in the case of the titrant, where relatively small temperature variations would cause loss of titrant (through the buret tip) due to expansion.

C. Operation of the Mark V Calorimeter.

The calorimeter was assembled as shown in Figure 11, except for the buret assembly which was added later. An appropriate volume of stock solution was pipetted into the calorimeter through the buret aperture and brought up to a constant volume by pipetting in distilled water assuming volume additivity.

The buret was connected to the titrant storage flask, the gears were disengaged, and the buret was filled by rotating the buret drive manually. Simultaneously the tip was washed out by allowing some titrant to flow through by



$\frac{1}{4}$ full scale.

Figure 11. The assembled calorimeter.

gravity feed. This volume varied from 5 to 25 ml., depending on the length of time between runs. The buret was then set by meshing the gears to the motor and turning the current on until about 0.1 ml. had been dispensed; this assured smooth delivery of the titrant from the beginning of the chemical run. The buret tip was carefully rinsed with distilled water and dried thoroughly with paper tissue. The buret was then mounted in place; the buret tip in the calorimeter and the buret counter bolted to a bracket mounted on the constant temperature bath.

The calorimetric determinations were done by performing the following operations.

1. The stirrer and the recorder were turned on.
2. The battery charger was turned off by opening switch A. (Figure 10).
3. Switches B and E were closed so that current was passing through the dummy heater.
4. The potential divider was set so that the heating rate of the electrical calibration would be about the same as that for the chemical run. This was done by estimating the enthalpy of the reaction, the rate of addition of titrant and calculating the rate of chemical heating.
5. The temperature of the calorimeter contents was adjusted such that the temperature after the addition of titrant would be $25 \pm 0.05^{\circ}\text{C}$. This temperature was estimated from the expected heat of reaction and the heat capacity of the calorimeter and its contents. If cooling was required, some powdered

dry ice was added to the cooling tube from a funnel, and the tube was evacuated with a vacuum pump. If heating was required, the calibration heater was used by closing switch C_1 . This meant that about 0.1 ml. or less of the titrant was at the starting temperature but this factor is negligible in its effect on the determination of enthalpy changes.

6. When the starting temperature had been attained, switch D was closed so that the buret motor would be activated when switch C_2 was closed.

7. There was a 15 minute fore-period, in which the temperature of the calorimeter contents rose about 0.03°C (due to heat of stirring and thermal leakage from the surroundings).

8. During the fore-period, the bath temperature, the room temperature, and the buret were read and recorded, and the electrical timer was set to zero.

9. At zero time, i.e. about 15 minutes after the temperature rise had become linear, switch C_2 was closed, activating the buret motor. Zero time was anticipated by using a stop-watch that had been synchronized with the time scale of the recorder chart paper.

10. After the desired amount of titrant had been added, the buret motor was turned off by opening switches C_2 and D.

11. There was a 20 minute after-period, in which the temperature rose about 0.02°C .

12. During the after-period, the bath temperature, the room temperature, the buret and the timer were read and recorded.

13. After about 20 minutes, the vacuum was released in the

cooling tube and dry ice was added to cool the calorimeter to the original starting temperature.

14. The apparatus and contents were now prepared for the calibration of the heat capacity of the calorimeter and its contents. During a 15 minute fore-period, the bath temperature, the room temperature, and the current through the dummy heater were read and recorded. The current was determined by balancing the potentiometer across the standard resistor, R_A . Since the resistance of R_A was 1.00000 ohms, the potential drop was numerically equal to the current in the heater circuit.

15. The electrical timer was set to zero.

16. At zero time, switch C_1 was closed and switch B was opened simultaneously so that the current was directed through the calibration heater rather than the dummy heater. Switch C_1 also activated the timer.

17. The current through the calibration heater was measured by determining the potential drop across R_A at 15 second intervals.

18. After the desired amount of heating of the calorimeter contents had been accomplished, switch C_1 was opened and switch B was closed simultaneously.

19. During a 20 minute after-period, the bath temperature, the room temperature and the time were read and recorded.

20. After about 20 minutes, the batteries were returned to charge and the calorimeter components were dismantled and rinsed thoroughly with distilled water.

D. Calculation of the Heat of Reaction.

Calculation of the heat dissipated by the chemical reaction was done by the method of Sturtevant (45). The temperature rise for the chemical run and the calibration run were determined from the recorded time-temperature curves illustrated in Figure 12 and Figure 13. T_R , the time at which the deflections were read, was chosen so that the areas A and B in Figure 12 were equal. The initial deflection, D_i , was determined by linearly extrapolating the fore-period to T_R with a straight edge. The final deflection, D_f , was determined by reading the deflection at 10 minutes and at 20 minutes in the after-period and algebraically extrapolating to T_R , e.g. if T_R was 1 minute, the deflection at 10 minutes was 120.0, and the deflection at 20 minutes was 125.0 divisions, then $D_f = 120.0 - \frac{5}{10} \times 9 = 115.5$ divisions.

The temperature rise in the chemical run, D_C , was then; $D_C = D_f - D_i$ divisions. The temperature rise in the calibration run, D_E , was; $D_E = D_f - D_i$ (from the calibration curve).

The heat released by the chemical reaction was then calculated from the following expression:

$$Q = \frac{D_C \times T_E \times R_H \times E^2}{D_E \times 4.1840 \times R_A^2} \quad \text{calories.}$$

Where T_E was the time in seconds that the current passed through the calibration heater, R_H was the resistance of the calibration heater, E was the potential drop across the stan-

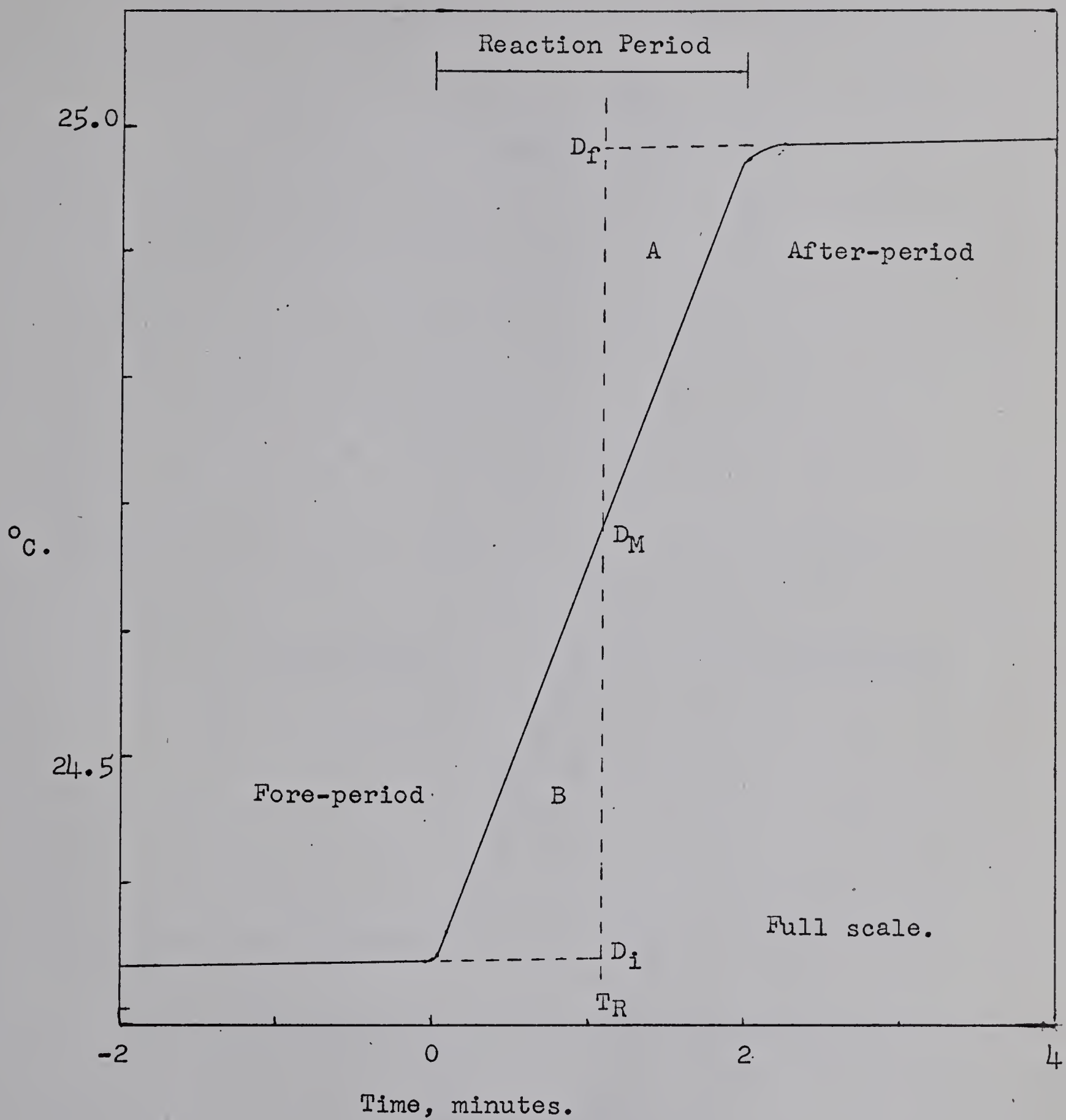


Figure 12. Typical chemical heating curve.

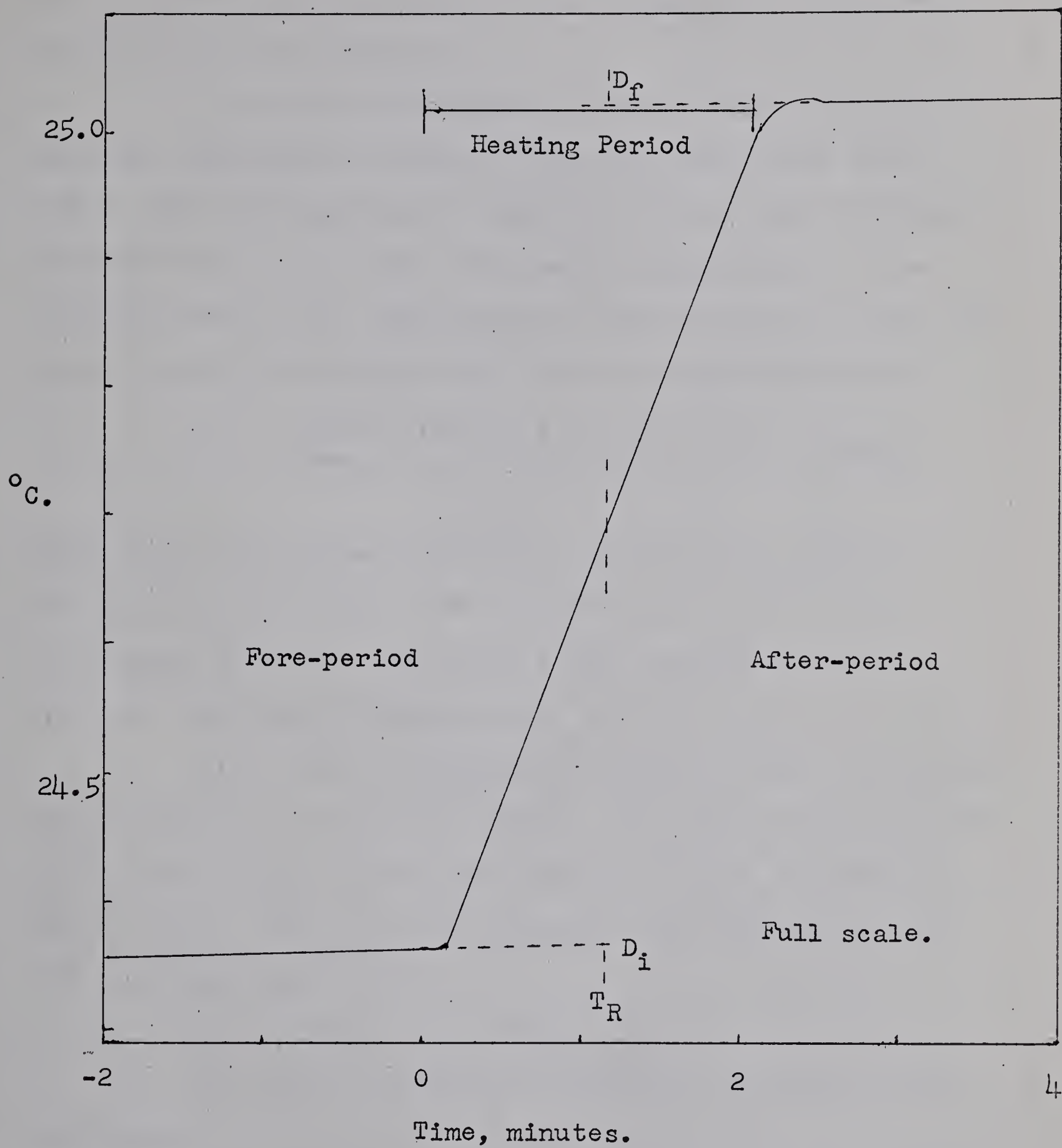


Figure 13 . Typical electrical calibration curve.

dard resistor R_A , and 4.1840 is the conversion factor from absolute joules to calories.

Since the temperature of the titrant was higher than the calorimeter contents, there was some extra heat added. The heat capacity of the $\text{HCl} \cdot 10 \text{ H}_2\text{O}$ was 0.756 calories per milliliter (80). The median temperature of the chemical heating, D_M , was chosen as the deflection at T_R . The correction was calculated from the following expression:

$$Q' = \frac{(D_{25} - D_M) \times V \times 0.756 \times 1000}{D_1} \text{ calories.}$$

Where V was the volume of titrant in liters, D_1 was the deflection produced by a 1°C difference in the bath and calorimeter contents, and D_{25} was the recorder deflection when the calorimeter contents were at 25°C .

There was a considerable amount of heat dissipated due to the dilution of the titrant. The heat of dilution was found from a graph constructed from the values reported by Rossini (81). The dilution correction was calculated from the following expression:

$$Q'' = \Delta H_{\text{dil}} \times V \times N \text{ calories.}$$

The heat of reaction, therefore, is given by the expression:

$$- \Delta H = \frac{Q - Q' - Q''}{V \times N} \text{ calories per mole.}$$

It can be seen from Figure 12 and Figure 13 that the chemical and electrical heating curves were almost identical. There was a slightly longer temperature lag at the

start and at the end of the electrical heating. This was due to the fact that the heat produced had to be conducted from the heater to the solution and from the solution to the thermocouples. The curves were so similar, however, that this difference was thought to cause little, if any, error in the heats determined.

E. Performance of the Mark V Calorimeter.

Before the calorimeter could be used for measurements of unknown enthalpy changes, it had to be tested by using it for measurement of an accurately known reaction.

The reaction chosen was $\text{NaOH} + \text{HCl} \rightarrow \text{NaCl} + \text{H}_2\text{O}$.

This reaction was extensively studied by T.W. Richards and A.W. Rowe (79).

1. Experimental.

An aqueous stock solution of carbonate-free sodium hydroxide was prepared in the following manner. A 50% by weight solution of NaOH in water was prepared and filtered through an asbestos pad with the aid of suction. The filtrate was diluted with freshly boiled distilled water so that the solution was 0.5 M in NaOH. The solution was stored in a paraffin coated bottle, and standardized against potassium hydrogen phthalate using phenolphthalein as an indicator.

A stock solution of $\text{HCl} \cdot 10 \text{H}_2\text{O}$ was prepared by weighing concentrated hydrochloric acid and the necessary distilled water on a triple beam balance. The solution was standardized by delivering a measured amount of the solution from the calorimeter buret and adding an excess silver nitrate.

The resulting AgCl was weighed and the concentration calculated.

The calorimetric determinations were done as previously described. A 5% excess of NaOH was used to eliminate any errors due to possible traces of carbonate formed during transfer of the solutions to the calorimeter.

The method of calculation used in the "D" runs was to multiply the ratio of the deflection, after three minutes of chemical run to electrical run, times the number of calories produced electrically. The method used in the "E" runs was to multiply the ratio of the areas under the curves, determined by weighing, times the calories produced electrically.

The results of the "F" calorimetric runs were calculated by the method of Sturtevant. In addition, they were corrected to 20°C using the temperature dependence of the reaction found by Richards and Rowe (79) and the temperature dependence of the heat of dilution of HCl found by Richards, Mair and Hall (80).

The results of three sets of runs, corrected to 20°C, are tabulated in Table 7. Assuming that the values of Richards represent the true heat of neutralization, the variances of the three calculation methods were not significantly different using the "F" test (82) as a criterion. The average of 21 runs agreed to within 3 calories per mole or 0.022% of the value found by Richards at 20°C, i.e.

$\Delta H_{20} \text{ experimental} = -13,777 \text{ calories/mole}$, $\Delta H_{20} \text{ Richards} = -13,774 \text{ calories/mole}$. The variation of the individual runs

TABLE 7.

THE HEAT OF NEUTRALIZATION OF SODIUM HYDROXIDE WITH HYDROCHLORIC ACID USING THE BURET TYPE CALORIMETER, AT 20° CENTIGRADE.

Run	Molality N _a Cl formed	ΔH , Richards - Calories	ΔH , Found - Calories	% Deviation
1 D	0.098	13,792	13,788	-0.03
2 D	0.098	13,792	13,778	-0.10
3 D	0.098	13,792	13,814	0.16
4 D	0.079	13,772	13,796	0.17
5 D	0.079	13,772	13,800	0.20
6 D	0.079	13,772	13,877	0.76
7 D	0.070	13,762	13,859	0.70
1 E	0.098	13,792	13,843	0.37
2 E	0.098	13,792	13,871	0.57
3 E	0.098	13,792	13,823	0.22
5 E	0.079	13,772	13,691	-0.59
6 E	0.079	13,772	13,791	0.14
7 E	0.059	13,748	13,708	-0.29
8 E	0.059	13,748	13,658	-0.65
9 E	0.059	13,748	13,646	-0.74
1 F	0.070	13,762	13,782	0.15
2 F	0.079	13,772	13,768	-0.03
3 F	0.079	13,772	13,697	-0.54
4 F	0.098	13,792	13,860	0.49
5 F	0.098	13,792	13,802	0.07
6 F	0.059	13,748	13,756	0.06

was much more pronounced (Figure 14 and Table 7). The 95% confidence limits were calculated by the method described in section E.3. The standard deviation of the mean should have been within 12 calories per mole, so the deviation found was somewhat fortuitous.

2. Statistical Treatment of Indeterminate Errors.

To calculate the heat of reaction, the following general equation was used.

$$-\Delta H = \frac{\frac{D_C \times T_E \times R_H \times E^2}{D_E \times 4.1840 \times R_A^2} - \frac{D_M' \times V \times 756}{D_1} + \Delta H_{dil} \times V \times N}{V \times N} .$$

Where

D_C , the recorder deflection for the chemical run.

D_E , the recorder deflection for the calibration run.

T_E , the time in seconds of electrical heating.

R_H , the resistance of the calibration heater.

E , the average potential across R_A during electrical heating.

R_A , the resistance of the standard resistor (1.00000 ohms).

D_M' , the median recorder deflection from 25°C during the chemical heating.

D_1 , the recorder deflection for 1°C.

V , the volume of titrant added (liters).

N , the normality of the hydrochloric acid.

ΔH_{dil} , the heat of dilution of hydrochloric acid.

The statistically calculated error of each of the factors in

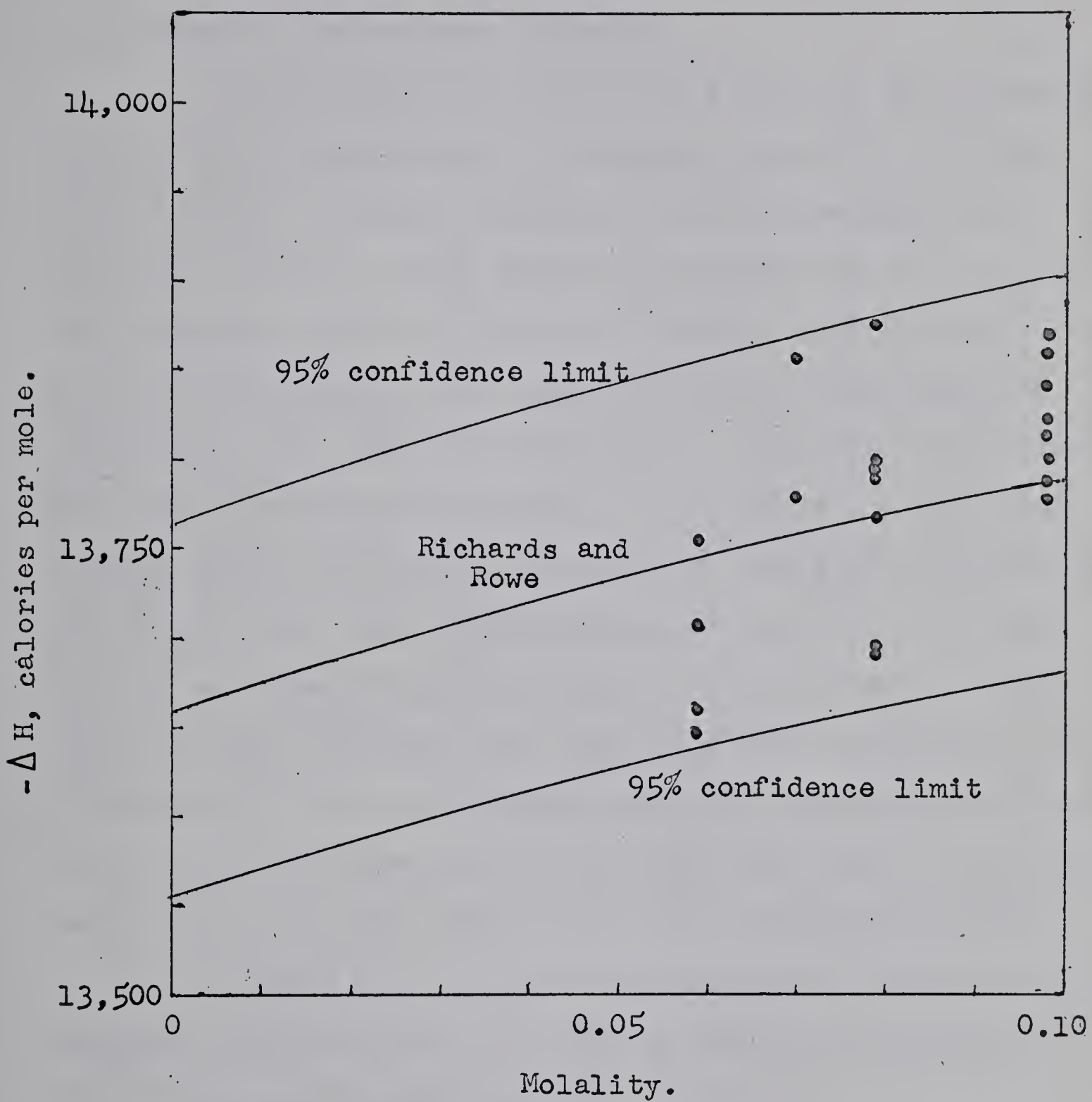


Figure 114. Heat of neutralization of sodium hydroxide by hydrochloric acid at 20° centigrade.

the preceding equation is listed in Table 8. The method of calculating these errors is described below.

a. Errors in the recorder response.

The potential drop across a 100.000 ohm standard resistor was measured with the Sargent model SR recording potentiometer. Using a Leeds and Northrop polarograph as the potential source, and a decade resistance box in series with the standard resistor to vary the current in the circuit, the potential drop across the standard resistor was measured accurately with a Rubicon Instruments model 2730 potentiometer. Zero deflection was determined by the method of least mean squares using 105 determinations at 21 different potentials. The median slope was found to be 26.34 divisions per millivolt at an attenuation of 10 millivolts full scale. The results at each potential have been plotted in Figure 15. The standard deviation of a single deflection determination was found to be 0.30 divisions between 25% and 75% of full-scale deflection, i.e. the range used in the calorimetric runs.

Since D_C and D_E were determined by three recorder readings, two of which were used to give D_f , the absolute error in D_C and D_E was therefore

$$s = \sqrt{(0.30)^2 + (0.30)^2} = 0.367 \text{ divisions.}$$

D_M was determined by a single reading, therefore
 $s = 0.30$ divisions.

D_1 was determined by 12 readings, therefore
 $s = 0.13$ divisions.

TABLE 8.

INDETERMINATE ERRORS.

Error Source	Symbol	Range	Standard Deviation	% Error Average
Recorder deflection	D_C, D_E	75 - 150	0.367 divisions*	0.33
Median deflection	D_M	30 - 70	0.30 divisions	0.60
Sensitivity	D_1	206.2	0.13 divisions	0.06
Calibration heater	R_H	98.525	0.005 ohms	0.005
Calibration time	T_E	100 - 150	0.057 seconds	0.05
Volume of titrant	V	3.0 - 7.0	0.0005 ml.	0.01
Normality of titrant	N	4.9117	0.0009 normal	0.02
Heat of dilution, HCl	ΔH_{dil}	- 1232	10 calories	0.81
Bath Temperature	T_B	25°C.	0.00056°C	0.10
Calibration voltage	E	0.25 - 0.35	0.00001 volts	0.003
Standard resistor	R_A	1.00000	0.00000 ohms	0.000

* The extra figures are used only for calculations of the confidence limits.

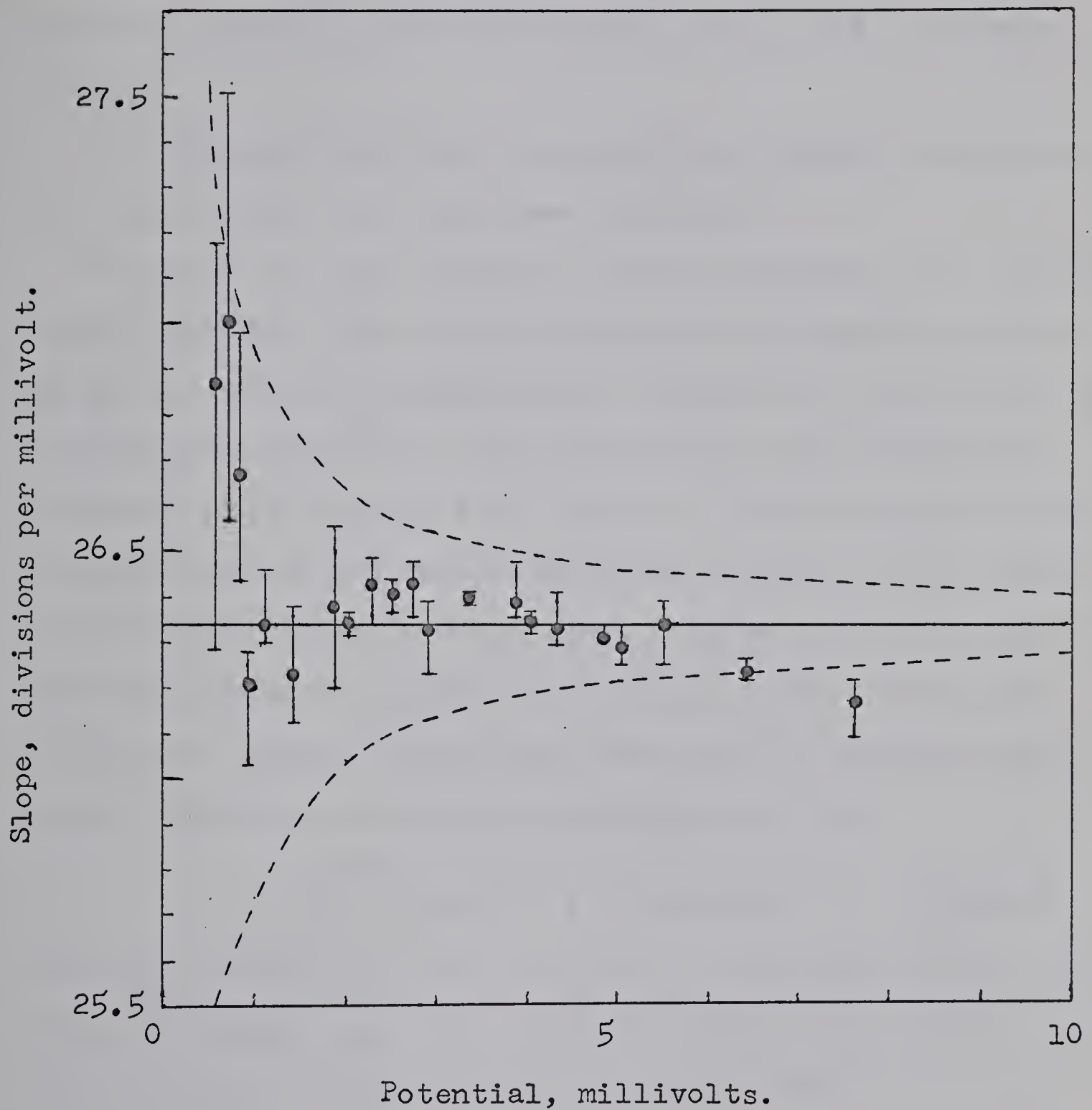


Figure 15. Error in the recorder response.

- median slope.
- 95% confidence limits, where the standard deviation of single reading was 0.30 div.
- median of five determinations.

The standard deviation of the bath temperature also affects these readings in a calorimetric run and therefore it has been included in the calculation of the 95% confidence limits.

b. The standard error of the calibration heater resistance was found to be 0.005 ohms (see Table 6).

c. The error in the volume of titrant delivered was estimated to be 0.0005 ml. The standard deviation of reading an ordinary 50 ml. buret by undergraduate students at the University of Alberta is 0.014 ml. This information was gratefully accepted from Professor W. E. Harris. The calorimeter buret could be read to two more significant figures but the smallest divisions were 0.002 ml. apart. It was therefore assumed that the standard deviation of a single buret reading was 0.00028 ml. Since two readings were used to determine the volume delivered the standard deviation of V was

$$s = \sqrt{(0.00028)^2 + (0.00028)^2} = 0.00039 \text{ ml.}$$

There was undoubtedly some backlash of the buret motor, and its contribution plus the standard deviation of reading the buret resulted in the estimated standard error in V, i.e. 0.0005 ml. If it is larger than this it has been included in the timing error.

d. The error in timing was determined in conjunction with forty chemical runs. Since both the time and the volume of titrant delivered were recorded for each run, it was possible to calculate the standard error of timing. For a flow-rate

of 2.5 ml. per minute, the following expression holds.

$$V = \frac{T}{24}, \text{ where } V \text{ is in ml. and } T \text{ is in seconds.}$$

The standard deviation of $\frac{24 \times V}{T}$ was found to be 0.00057 ml.

per second, therefore

$$\frac{(0.00057)^2}{1^2} = \frac{s^2}{120^2} + \frac{(0.0005)^2}{(5.0000)^2} + 0, \text{ where } s$$

is the standard error in the time in seconds. The standard error in the time was, therefore, 0.067 seconds.

e. The standard deviation of the concentration of hydrochloric acid was 0.0009 molar, found by potentiometrically standardizing the acid against sodium carbonate. Molality was used in Table 7 so that the Mark IV and Mark V runs could be compared.

f. The uncertainty of the heat of dilution of the titrant due to small differences in the final concentration and due to the fact that the value for a particular run was taken from a graph was estimated to be 10 calories per mole.

g. The standard deviation of the bath temperature was found from 30 runs (120 readings) using a Beckman thermometer to be 0.00056°C.

h. The error in reading the potentiometer was estimated to be 0.03 millivolts. Since about 10 readings were made for each run, the standard deviation of the potential drop across R_A was 0.01 millivolts.

i. Although it was not used in the calculation of the 95% confidence limits, it is of interest to note that the room

temperature was controlled at $25 \pm 0.5^{\circ}\text{C}$.

3. Calculation of the 95% Confidence Limits.

The 95% confidence limits for a single calorimetric run were calculated in the following manner. The equation for calculating ΔH as shown above was divided into 4 components, i.e.

$$\text{a. } \frac{D_C \cdot T_E \cdot R_H \cdot (E)^2}{D_E \cdot 4.1840 \cdot (R_A)^2}$$

$$\text{b. } \frac{D_M \cdot V \cdot N \cdot 163}{D_1}$$

$$\text{c. } \Delta H_{\text{dil}} \cdot V \cdot N$$

$$\text{d. } V \cdot N$$

The relative error of each of the components was calculated. The relative errors of a, b, and c were converted to absolute errors and the absolute error of the numerator was calculated, and converted to relative error. The relative error of the enthalpy was then calculated.

The following data were obtained for the neutralization of glycinate anion.

$$D_C = 110.2 \text{ divisions}$$

$$D_E = 106.5 \text{ divisions}$$

$$D_M = 54.0 \text{ divisions}$$

$$T_E = 143.27 \text{ seconds}$$

$$E = 0.29605 \text{ volts}$$

$$V = 5.0112 \text{ ml.}$$

$$N = 4.9117 \text{ normal}$$

$$\Delta H_{\text{dil}} = -1232 \text{ calories per mole}$$

These data yield the following:

$$a = -305.97 \text{ calories}$$

$$b = -1.05 \text{ calories}$$

$$c = -30.32 \text{ calories}$$

$$d = 0.024614 \text{ moles}$$

$$\Delta H = -11,156 \text{ calories}$$

Calculation of the 95% confidence limits for this run follows:

$$\begin{aligned} \left(\frac{s_a}{a} \right)^2 &= \left(\frac{\sqrt{(0.367)^2 + (0.1)^2}}{110.2} \right)^2 + \left(\frac{\sqrt{(0.367)^2 + (0.1)^2}}{106.5} \right)^2 + \left(\frac{0.067}{143.27} \right)^2 + \\ &\quad \left(\frac{0.00001}{0.29605} \right)^4 + \left(\frac{0.005}{98.525} \right)^2 + 0 + 0 \\ &= 0.00002478 \end{aligned}$$

$$s_a = 1.52 \text{ calories}$$

$$\begin{aligned} \left(\frac{s_b}{b} \right)^2 &= \left(\frac{\sqrt{(0.30)^2 + (0.1)^2}}{54.0} \right)^2 + \left(\frac{\sqrt{(0.13)^2 + (0.1)^2}}{206.2} \right)^2 + \left(\frac{0.0005}{5.0112} \right)^2 + \left(\frac{0.0009}{4.9117} \right)^2 \\ &= 0.00003216 \end{aligned}$$

$$s_b = 0.0060 \text{ calories}$$

$$\begin{aligned} \left(\frac{s_c}{c} \right)^2 &= \left(\frac{10}{1232} \right)^2 + \left(\frac{0.0005}{5.0112} \right)^2 + \left(\frac{0.0009}{4.9117} \right)^2 \\ &= 0.000006593 \end{aligned}$$

$$s_c = 0.246 \text{ calories}$$

$$\left(\frac{s_d}{d}\right)^2 = \left(\frac{0.0005}{5.0112}\right)^2 + \left(\frac{0.0009}{4.9117}\right)^2 = 0.000000043$$

$$s_{abc} = \sqrt{(1.52)^2 + (0.006)^2 + (0.246)^2} = 1.54 \text{ calories}$$

$$s_{abc} = 0.00561$$

$$\frac{s_{\Delta H}}{\Delta H} = \sqrt{0.000031472 + 0.000000043} = 0.56 \%$$

The 95% confidence limits were therefore 1.10%.

Under similar conditions, allowing for the increase of D_C and D_E due to greater evolution of heat, the 95% confidence limits for the neutralization of sodium hydroxide were found to be 0.80% or 110 calories. The 95% confidence limits and the probable deviation due to indeterminate errors are shown for various values of enthalpy in Figure 16. From this figure, one can ascertain the probable deviation for a single run.

The example calculated chosen at random from the experimental run, falls above the line because D_E was numerically smaller than D_C , whereas the curves for Figure 16 were calculated assuming $D_C = D_E$. Conversely if D_E was greater than D_C , the limits would be somewhat improved.

The standard deviation of determining the heat capacity of the calorimeter and contents should be about 0.37% or for most runs considered, $s = 2.12$ calories. The standard deviation of adding the contents was estimated to be 1.5 ml.

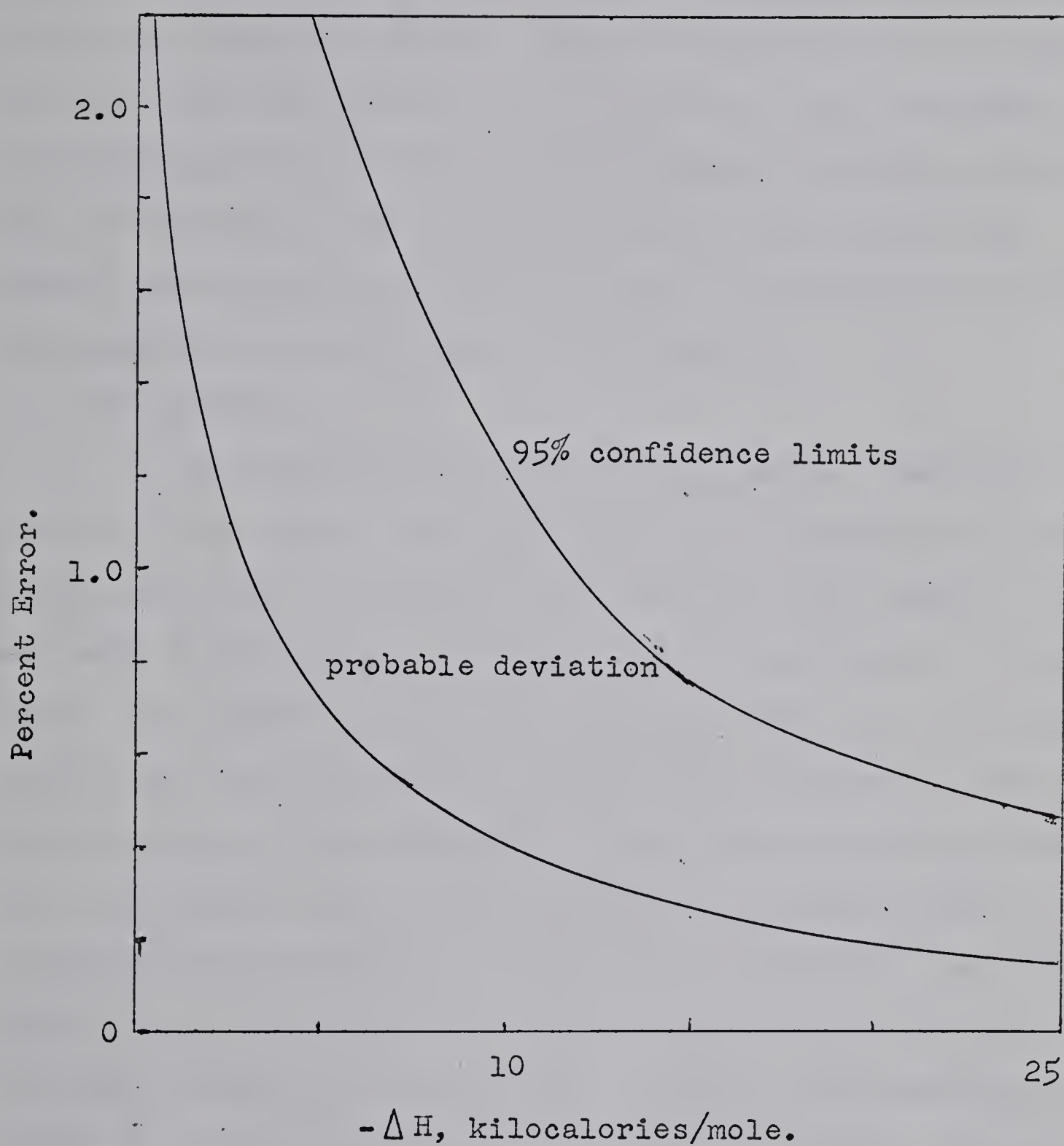


Figure 16. Confidence limits of calorimetric determinations for a single run, due to indeterminate errors.

or 0.3%, since the additions were not made by strictly quantitative methods and for some runs the apparatus was not completely dry when assembled. These variations would be identical for both the chemical and calibration runs. However, considering these two factors, the standard deviation would be 2.60 calories. The standard deviation was found from twenty-seven runs to be 2.58 calories, considered to be excellent agreement for this type of calculation.

F. CONCLUSIONS.

In view of the preceding information, the calorimeter and the method used were considered adequate for determining the heats of reaction considered in this thesis. There are some disadvantages in working with a calorimeter of this type. The sensitivity of the thermopile was such that relatively high concentrations of titrant were required. This was not a serious problem with HCl, since the concentration used was sufficiently high, almost exactly the concentration of constant-boiling $\text{HCl} \cdot \text{H}_2\text{O}$, and the heat of dilution and heat capacity are well known. The values found were for ionic strengths between 0.10 and 0.20, which for some reactions may differ significantly from the enthalpy at infinite dilution. This disadvantage could be partially overcome by using thermistors or a resistance thermometer. The use of thermocouples, however, provided the simplest temperature sensing device.

The Teflon supports did not reach thermal equilibrium as rapidly as was desired, and if supports which have a low heat capacity combined with high thermal conductivity could be

used, the length of the fore and after periods could be shortened significantly.

The polyurethane coating was attacked by amines if they came out of solution. This occurred once when using n-hexylamine, but when the concentration was diminished so that the amine was soluble, no further attack took place. The use of polyurethane, however, minimized the lag of the temperature response to about three seconds for both the chemical and calibration runs, which is superior to the designs in which the thermometer and heater are encased in glass tubes.

III. EXPERIMENTAL

A. MONOAMINES

1. Source and Purity.

The monoamines were obtained from various sources and are listed together with the sources in Table 9. Some were obtained in the form of the hydrochloride and were used without further purification to make up stock solutions. The amines which were not in the salt form were analyzed by gas chromatography.

The chromatography column was an eight foot long, 0.25 inch diameter copper tube packed with hexamethyldisilizane - treated Chromosorb W coated with 20% SE-30 silicone gum rubber (Chromatographic Specialties). The column was wound around a cylindrical aluminum block which had a thermometer well and a heater well into which fitted a pencil heater which was controlled by a variable transformer. The column assembly was completely insulated with glass wool. A preheater was used to heat the eluant gas to well above the boiling point of the sample by controlling the preheater temperature with a variable transformer. The preheater consisted of a copper coil wrapped with an electrical heating tape and insulated with asbestos tape. The detection device was a Gow-Mac Instruments model TR2B thermal conductivity cell in conjunction with a Gow-Mac Instruments model 9999C power supply. The recorder was a Sargent model SR recording potentiometer equipped with an attenuator which allowed the range to be set from 1 millivolt to 30 volts full-scale

Table 9.

SOURCE AND PURITY OF MONOAMINES

Amine	Source*	Chromatographic Data		Impurities #
		Temperature °C	% Impurity	
Ammonia	1s			
Methylamine	2s			
Ethylamine	3s			
n Propylamine	3	45	0.01	1
n Butylamine	3s			
n Pentylamine	4	161	0.03	1
n Hexylamine	3	161	0.1	4
i Propylamine	3	46	0.03	3
i Butylamine	3	90	0.00	0
s Butylamine	4	94	0.3	2
t Butylamine	3	83	0.01	1
Allylamine	3	49	0.2	6
Benzylamine	3	155	0.2	1
Phenethylamine	3	155	0.9	9
Methylbenzylamine	3	215	0.1	4
Dimethylamine	5s			
Diethylamine	3s			
Di-n-propylamine	3	129	0.6	3
Pyrrolidine	6	134	0.5	2
Piperidine	3	161	0.0	0
Trimethylamine	3			
Triethylamine	5	105	2.5	6

- *1. Baker and Adamson
 2. Fisher Scientific
 3. Eastman Organic Chemicals
 4. Matheson Co.
 5. British Drug Houses
 6. Aldrich Chemical Co.

deflection in ten steps.

The chromatographic determinations were carried out in the following way. The column was heated to a suitable temperature depending on the boiling point of the amine i.e. the higher the boiling point, the higher the column temperature. The carrier gas was helium and its flow-rate was 60 ml. per minute. The sample used was 2 microlitres of the liquid amines. With a sample of this size the parent peak was recorded using an attenuation of 100 millivolts, while the rest of chromatogram was recorded using an attenuation of 1 millivolt, i.e. the sensitivity was 100 times as great for the impurity peaks as it was for the parent peak. Some typical chromatograms are shown in Figure 18.

In calculating the percent impurity it was assumed that the impurities had the same thermal conductivity response as the amine analyzed. The percentage impurity was calculated by dividing the sum of the areas of the impurity peaks by the total peak area (determined by counting squares) and multiplying by 100. This data along with the number of impurities are listed in Table 9. The effect on the heat of protonation of selected impurities is illustrated at the end of the experimental section.

2. Preparation of Salts and Stock Solutions.

The hydrochlorides of the amines not already in this form were prepared by bubbling HCl gas through di ethyl ether solutions of the amines. After the reaction was about 80% complete, the white crystals were filtered off with the

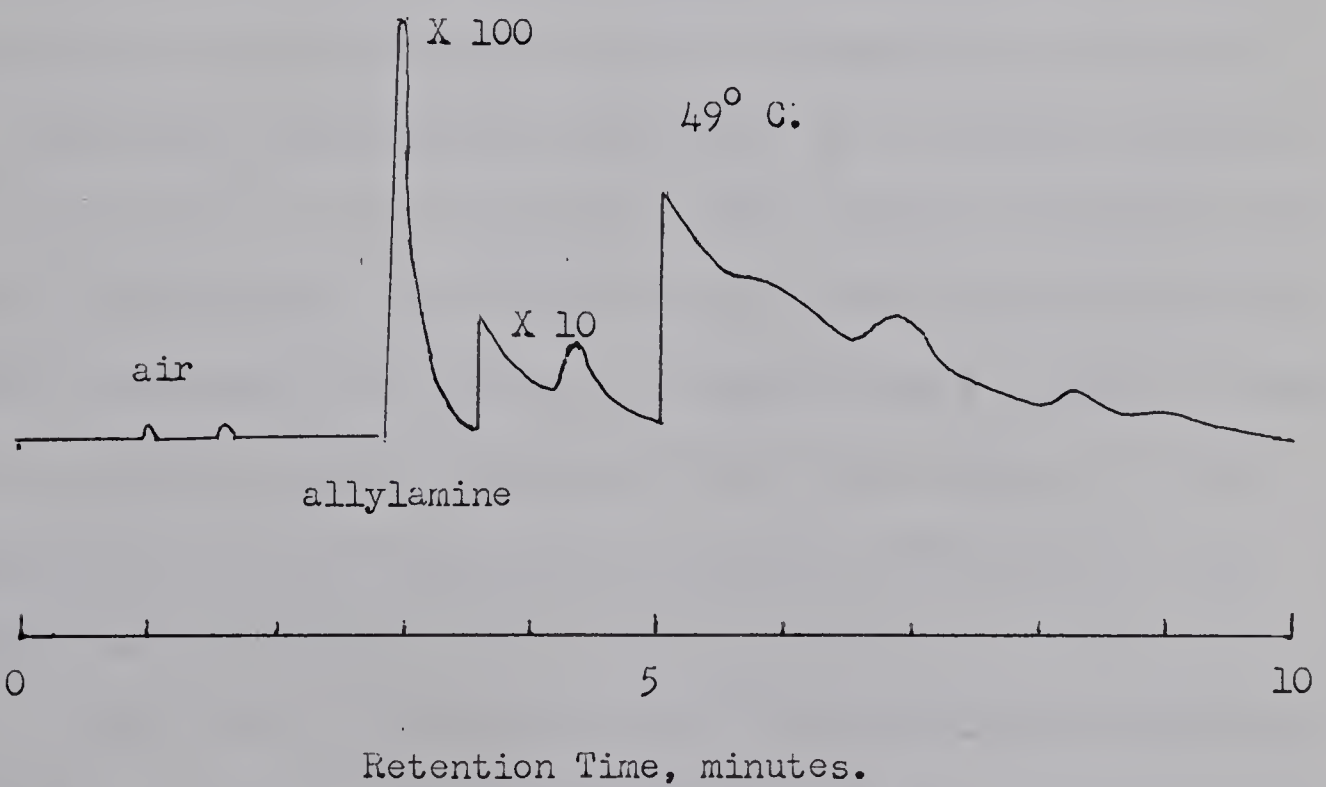
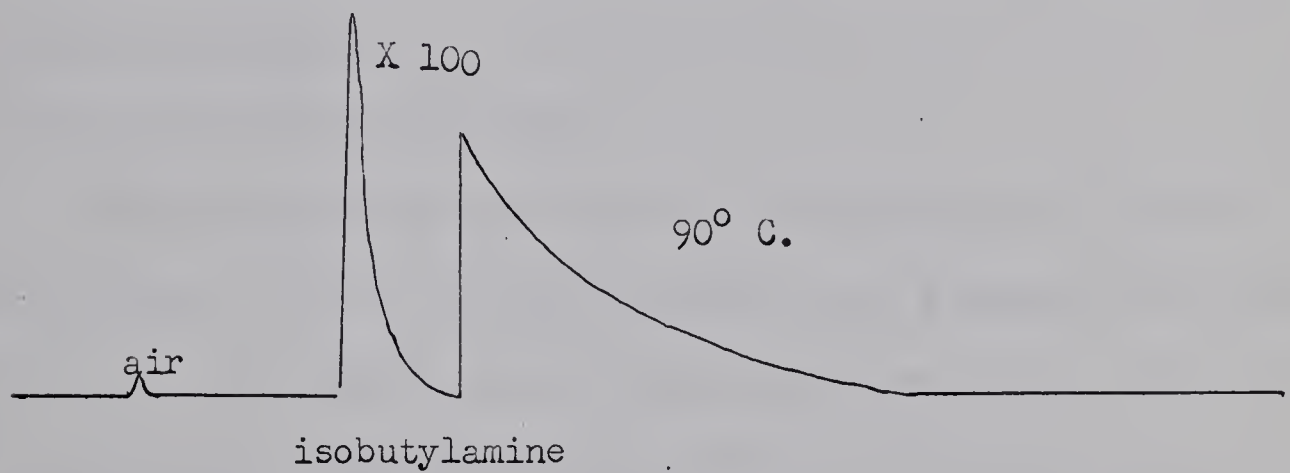
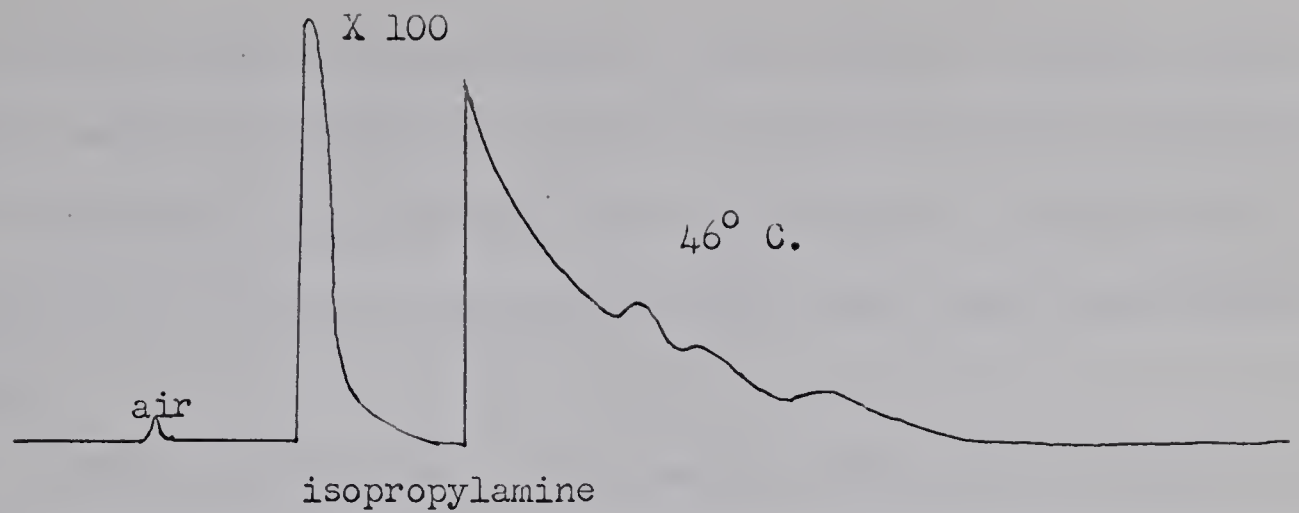


Figure 18. Chromatograms of some monoamines.

aid of suction and washed several times with diethyl ether. The salts were air-dried for several hours with the exception of the allylamine, piperidine, and pyrrolidine salts which were dried in a vacuum desiccator since they were very deliquescent.

Stock solutions of the amine salts were prepared by weighing the amount required to make a 0.500 molar solution and diluting to volume in volumetric flasks with freshly boiled distilled water.

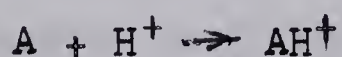
3. Calorimetric Determinations.

The calorimeter was set up as described in the previous section. The initial solution was prepared by pipetting 100 ml. of 0.500 M amine salt stock solution, 325 ml. of distilled water, and 50 ml. of 0.75 M carbonate-free sodium hydroxide into the calorimeter. The buret assembly was attached, the temperature of the contents was adjusted so that the final temperature would be $25 \pm 0.05^{\circ}\text{C}$, by estimating the heat of protonation of the species involved and the fore-period begun. At zero time, 4.9117 M hydrochloric acid was introduced at a rate of 2.500 ml. per minute. After 5.0 ml. had been added, the buret motor was stopped. All other operations were identical to those performed in the NaOH + HCl experiments.

The ratio of free amine to the protonated species initially was 3 to 1, and finally was 1 to 3. These conditions have some very great advantages. The stability constants did not have to be known with any great accuracy, since

the amount of the reaction $\text{H}^+ + \text{OH}^- \rightarrow \text{H}_2\text{O}$ was minimized and, therefore, also the correction for this reaction was diminished. If there were other amine impurities the error in the heat of protonation due to impurities would have been decreased because of differences in the stability constants, i.e. if the stability constants of the impurities were greater than that of the amine in question, they would have already been protonated to a larger degree in the initial solution, and if they were smaller they would have become protonated to a lesser degree during the calorimetric run.

In calculating the heats of protonation, the heat of neutralization of OH^- was taken as -13.36 kilocalories per mole (81) and the heat of dilution of hydrochloric acid in going from $\text{HCl} \cdot 10.16 \text{ H}_2\text{O}$ to $\text{HCl} \cdot 1080 \text{ H}_2\text{O}$ was taken as 1232 calories per mole (81). The results for the reaction



are tabulated in Table 10. The values refer to the heat of neutralization at ionic strength of 0.155. The values of the free energy have been calculated from selected stability constants from the literature¹ and the entropy from the enthalpy and the free energy. It can be argued that since the concen-

1. The stability constants used for the calculation of ΔF were selected from the values reported in the literature which were determined at 25°C. Where numerous values were reported preference was given to those which were extrapolated to infinite dilution and which seem to have been determined most accurately. Preference was also given to those values reported for a series of compounds in one publication e.g. those reported by Hall, J. Am. Chem. Soc., 79 5441 (1957).

Although few of the values selected were determined under the conditions used in this study, no attempt was made to correct them, for instance by applying the Extended Debye-Huckel Equation, since it was felt that no correction was preferable to an uncertain one.

tration of HCl was infinitely dilute at all times, the heat of dilution correction should have been 1340 calories per mole. This would mean that the enthalpies in Table 10 would be 0.11 kilocalories per mole less exothermic. Since there should also be included a correction for the dilution of the other components in solution and since these are not known it was decided that the reported values should be left uncorrected (to infinite dilution) rather than attempting to use uncertain correction terms. It is interesting to note, however, that when the HCl dilution correction has been made, five of the ten values that can be compared agree within 0.1 kilocalories per mole with the values determined by the temperature dependence of the stability constant as quoted by Bell (56) is shown in Table 10.

In the case of the protonation of ammonia difference between calorimetric and temperature dependence results was unusually large. A series of runs was performed at various concentrations i.e. using different amounts of HCl, NH_4Cl and NaOH such that the ratios of the components was maintained constant so that the initial and final pH of all runs would be the same. The results of this study are shown in Figure 19. Included are the results of Tyson, McCurdy and Bricker, Bates and Pinching, and Everett and Landsman. The upper curve was drawn using the experimental results corrected by using the heat of dilution of HCl to the final concentration. The lower curve was drawn after applying the correction to infinite dilution of HCl and since it was linear

TABLE 10.

THERMODYNAMIC DATA FOR THE PROTONATION OF MONOAMINES, AT 25°C.

	$-\Delta F$	$-\Delta H$	ΔS	$-\Delta H(\text{Bell})$	Reference
	kilocalories/mole		e.u.	kcal./mole	
Ammonia	12.61	12.73	-0.40	12.40	83
Methylamine	14.49	13.35	3.82	13.09*	83
Ethylamine	14.50	14.31	0.64	13.58	83
n Propylamine	14.37	14.04	1.11	13.85*	83
n Butylamine	14.45	14.26	0.64	14.07*	83
n Pentylamine	14.50	14.37	0.44		84
n Hexylamine	14.54	14.53	0.03		84
i Propylamine	14.50	14.08	1.41		83
i Butylamine	14.23	14.10	0.44		85
s Butylamine	14.41	14.29	0.40		83
t Butylamine	14.26	14.42	-0.53		83
Allylamine	12.95	13.15	-0.67		83
Benzylamine	12.74	13.12	-1.27		83
Phenethylamine	13.41	13.50	-0.30		83
Methylbenzylamine	12.89	13.19	-1.01		86
Dimethylamine	14.52	12.31	7.41	11.88	83
Diethylamine	14.98	12.96	6.77	12.77*	83
Di n propylamine	15.01	13.43	5.30		83
Pyrrolidine	15.38	13.50	6.31		83
Piperidine	15.31	13.07	7.51	12.80*	83
Trimethylamine	13.32	8.91	14.79	8.83	83
Triethylamine	14.53	10.64	13.05	12.21	83

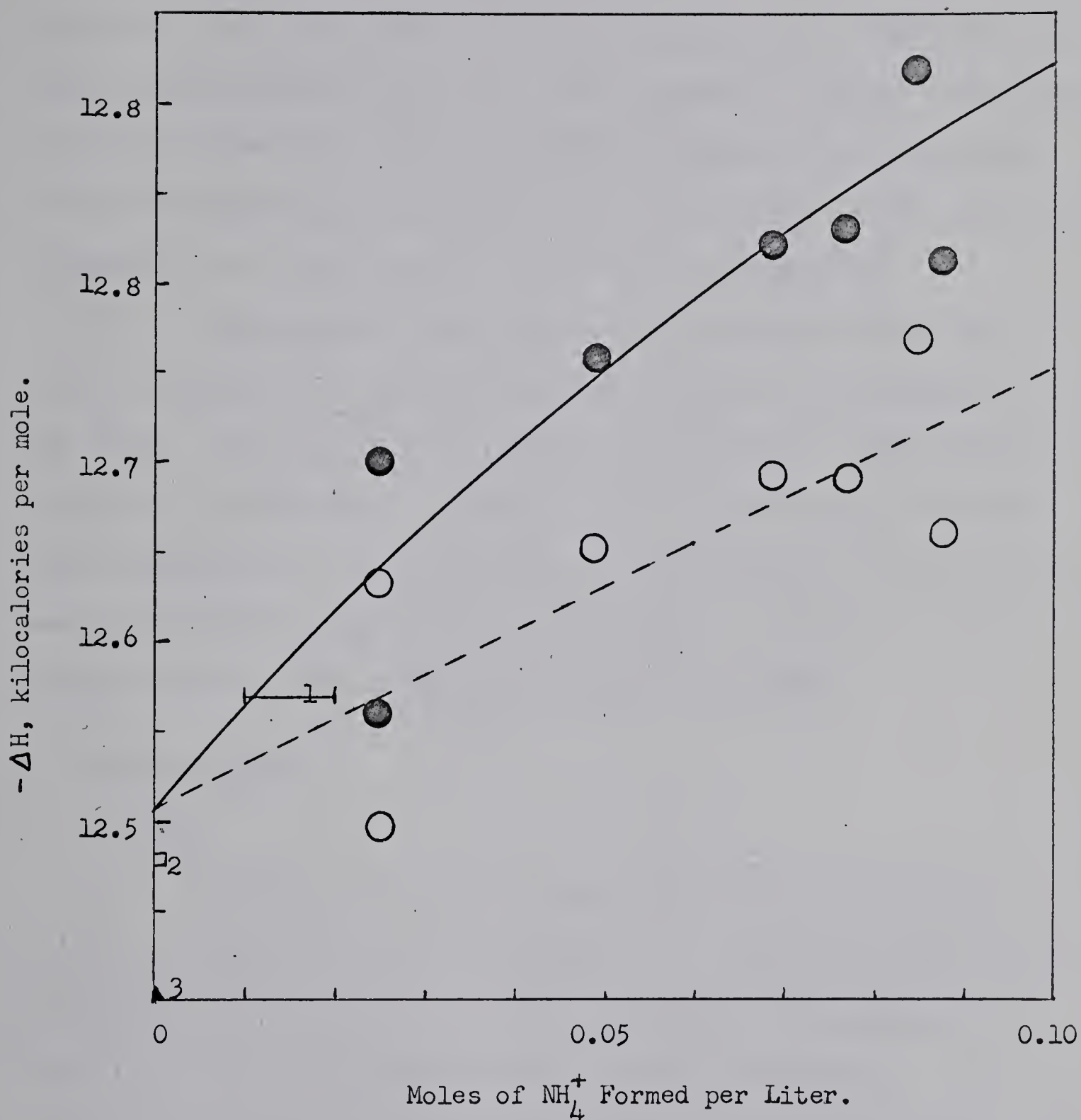


Figure 19. Heat of protonation of ammonia at various concentrations.

● — experimental.

○ - - - experimental, corrected to infinite dilution of HCl.

1. Tyson, B.C., W.H. McCurdy and C.E. Bricker, *Anal. Chem.*, 33, 1640 (1961).
2. Bates, R.G., and G.D. Pinching, *J. Res. Nat. Bur. Standards*, 42, 419 (1949).
3. Everett, D.H. and D.A. Landsman, *Trans. Faraday Soc.*, 50 1221 (1954).

the method of least mean squares was used. The value of ΔH found was -12.51 kilocalories per mole. The agreement is excellent with the value reported by Bates and Pinching i.e. -12.478 kilocalories per mole but somewhat higher (0.11 kilocalories per mole) than the value reported by Everett and Landsman. This difference plus the HCl dilution factor occur relatively frequently as indicated by asterisks in Table 10.

The probable deviation for a single determination in the series of monoamines was found to be 0.04 kilocalories per mole. On the average, this corresponds to 95% confidence limits of 0.88% which is almost exactly the value forecast from Figure 16. Since the heat of protonation of each amine was determined in duplicate, the values in Table 10 should be precise within 95% confidence limits of 0.62%.

B. AMINO ACIDS.

1. Source

A series of amino acids was obtained from various sources which are listed in Table 11. Cysteine and N isopropylglycine were obtained as the hydrochloride salts, while the others were obtained as the neutral compounds. The amino acids were used without further purification to prepare stock solutions. The effect of impurities on the heats of protonation will be illustrated by examples at the end of the experimental section.

2. Preparation of Stock Solutions.

Stock solutions of the amino acids were prepared

Table 11.

SOURCE OF AMINO ACIDS.

Amino acid	Chemical name	Source*
Glycine	aminoacetic acid	1
2 alanine	2 aminopropionic acid	1
2 aminobutyric acid	same	1
Norvaline	2 aminopentanoic acid	1
Valine	2 amino-2-isopropylacetic acid	2
Phenylalanine	2 amino-3-phenylpropionic acid	1
Serine	2 amino-3-hydroxypropionic acid	1
Cysteine	2 amino-3-mercaptopropionic acid	1
2 methylalanine	2 amino-2-methylpropionic acid	1
3 alanine	3 aminopropionic acid	3
3 aminobutyric acid	same	4
4 aminobutyric acid	same	4
Sarcosine	N methylaminoacetic acid	5
NN dimethylglycine	NN dimethylaminoacetic acid	5
Proline	pyrrolidine α carboxylic acid	2
N isopropylglycine	N isopropylaminoacetic acid	6

- *1. Eastman Organic Chemicals
- 2. Nutritional Biochemicals Corporation
- 3. General Biochemicals
- 4. Aldrich Chemical Co.
- 5. Chemical Procurement Laboratories
- 6. Frinton Laboratories

by weighing the amount required to make a 0.25 M solution and diluted to volume in a volumetric flask with distilled water. In the case of cysteine and N isopropylglycine, the appropriate amount of carbonate-free sodium hydroxide was added to neutralize the acid salt.

3. Calorimetric Determinations.

The calorimetric determinations were done in a manner similar to that used for the monoamines to obtain the heat of protonation of the amino group. The results are tabulated in Table 12. The values of the free energy have been calculated from selected stability constants from the literature and the entropy from the enthalpy and the free energy.

The probable deviation of a single determination of the heat of protonation of the amino group for the series of amino acids was found to be 0.05 kilocalories per mole. on the average this corresponds to 95% confidence limits of 1.37%. Since each amino acid heat of protonation was determined in duplicate, the values in Table 12 should be precise within 95% confidence limits of 0.96%.

The heat of protonation of the carboxylate group was determined in a somewhat different manner. After the determination of the heat of protonation of the amino group had been completed, the calorimeter contents were cooled, and following a fifteen minute fore-period, hydrochloric acid was added at a rate of 2.500 ml. per minute until 5 ml. had been added. After the protonation of the amino group

Table 12.

THERMODYNAMIC DATA FOR THE PROTONATION OF THE AMINO GROUP ON
AMINO ACIDS, AT 25°C.

Amino acid	$-\Delta F$ kilocalories/mole	$-\Delta H$	ΔS e.u.	Reference
Glycine	13.10	11.13	6.61	55
2 alanine	13.22	11.08	7.51	87
2 aminobutyric acid	13.71	11.10	8.75	88
Norvaline	13.23	11.15	6.98	89
Norleucine	13.32	11.16	7.24	90
Valine	13.13	11.00	7.14	89
Phenylalanine	12.46	10.93	5.13	91
Serine	12.48	10.58	6.37	91
Cysteine	11.41	8.48	9.83	92
2 methylalanine	(13.5)	11.84	(5.6)	-
3 alanine	13.62	11.66	6.57	90
3 aminobutyric acid	(13.6)	11.38	(7.4)	-
4 aminobutyric acid	14.40	12.48	6.44	93
Sarcosine	13.66	10.11	11.91	55
NN dimethylglycine	13.37	7.94	18.21	55
Proline	14.57	10.32	14.25	90
N isopropylglycine	13.73	10.28	11.57	55
(estimated)				

was complete, there was a change slope of the heating curve corresponding to the protonation of the carboxylate group as illustrated in Figure 20. The after-period was extrapolated back to about -8 minutes, and similarly the slope of the carboxylate portion was extrapolated back using linear extrapolation in both cases. The slope was determined in divisions per minute. The heat capacity was determined in conjunction with twenty-seven runs and found to be 2.81 calories per division. The enthalpy was then calculated using the expression:

$$\Delta H = \frac{S \times 2.81 - \Delta H_{\text{dil}}}{2.500 \times N} \times 0.0025 \times N \text{ kilocalories/mole.}$$

The results are tabulated in Table 13. The values of the free energy have been calculated from selected values of the stability constants from the literature and the entropy from the enthalpy and the free energy.

It is readily apparent from Figure 16 that at an optimum value of the heat of reaction it would be advantageous to use the slope method of calculating ΔH rather than the conventional method. The slope method is most accurate for small values of ΔH , i.e. if the slope was small, the absolute error in measuring the slope would be small, however if the slope was large the error in measuring the slope would be large. The probable deviation of a single determination of the heat of protonation of the carboxylate group was found to be 0.01 kilocalories per mole. On the average this corresponds to 95% confidence limits of 4.5%. Since

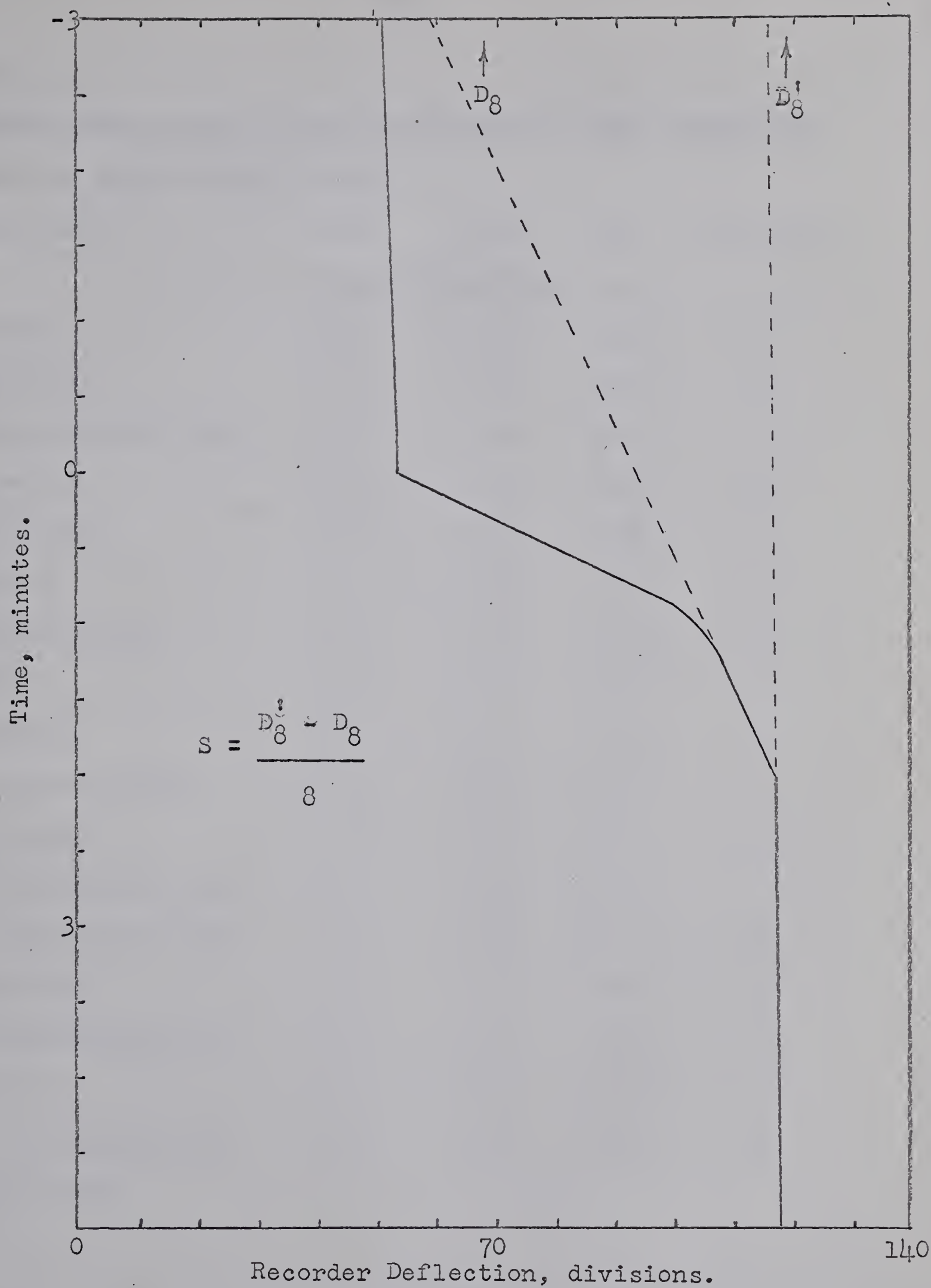


Figure 20. Typical heating curve for the protonation of the carboxylate group of amino acids

Table 13.

THERMODYNAMIC DATA FOR THE PROTONATION OF THE CARBOXYLATE
GROUP ON AMINO ACIDS, AT 25°C.

Amino acid	$-\Delta F$	$-\Delta H$	ΔS	Reference
	kilocalories/mole		e.u.	
Glycine	3.19	1.03	7.24	55
2 alanine	3.19	0.75	8.18	87
2 aminobutyric acid	3.15	0.32	9.49	88
Norvaline	3.12	0.36	9.26	89
Norleucine	3.07	0.57	8.38	90
Valine	3.17	0.25	9.79	89
Phenylalanine	3.10	0.55	8.55	91
Serine	3.00	1.16	6.17	91
Cysteine	2.67	0.53	7.18	92
2 methylalanine	(3.2)	0.53	(9.0)	-
3 alanine	4.78	1.17	12.11	90
3 aminobutyric acid	(5.0)	0.96	(13.5)	-
4 aminobutyric acid	5.50	0.58	16.57	93
Sarcosine	3.06	0.80	7.58	55
NN dimethylglycine	2.84	0.47	7.95	55
Proline	2.63	0.01	8.79	90
N isopropylglycine	3.22	1.00	7.45	55
(estimated)				

each run was done in duplicate, the values in Table 13 should be precise within 95% confidence limits of 3.2%

C. DIAMINES.

1. Source and Purity.

A series of diamines was obtained from various sources which are listed in Table 14. The diamines were distilled through a four inch column at 700 mm. Hg, the first 25% of the distillate was discarded and the next 50% was used for the experimental determinations. The boiling range for each amine appears in Table 14. The boiling points found agree well with those reported by Basolo and co-workers and with other literature values. The distilled diamines were stored in flasks sealed with serum caps.

The diamines were titrated potentiometrically with hydrochloric acid using the calorimeter buret. The percent titratable amine based on the value of the pure, anhydrous compound is reported in Table 15. Since the amines were extremely hygroscopic, there was a relatively large amount of water in the distilled amines.

Using the chromatographic technique described for the monoamines, the purity of all the diamines except NN' dimethylethylenediamine were at least 99% pure (excluding water as an impurity) as is shown in Table 14. In the case of NN' dimethylethylenediamine, it was found that the impurity was not due to any of the diamines in the series considered but the titration showed that it was diacidic, i.e. the

TABLE 14.

SOURCE AND PURITY OF DIAMINES

Diamine	Source*	B.P.	Chromatographic data		
		°C	Temp.	%imp.	#imp.
Ethylenediamine	1	113.8	115	0.1	2
1,3 diaminopropane	2	135.6	156	0.2	3
1,4 diaminobutane	2	156.8	160	0.8	4
1,2 diaminopropane	3	117.0	156	0.5	1
1,2 diamino-2-methylpropane	2	120.0	161	0.2	4
N methylethylenediamine	4	109.8	159	0.1	2
NN dimethylethylenediamine	2	101.6	156	0.3	1
NN' dimethylethylenediamine	2	111.7	157	14.35	5
NNN'N' tetramethylethylenediamine	1	118.9	155	0.05	5

- *1. Eastman Organic Chemicals
 2. Aldrich Chemical Co.
 3. K & K Laboratories
 4. Chemical Procurement Laboratories

TABLE 15.

HEAT OF SOLUTION OF DIAMINES

Diamine	% diamine titratable	$-\Delta H_{\text{sol}}$ kilocalories/mole	$-\Delta H_{\text{corr}}$
Ethylenediamine	98.0	8.70	9.06
1,3 diaminopropane	98.26	8.52	8.82
1,4 diaminobutane	96.04	8.46	9.17
1,2 diaminopropane	97.24	7.57	8.01
1,2 diamino-2-methylpropane	94.44	9.04	10.14
N methylethylenediamine	87.05	7.94	10.48
NN dimethylethylenediamine	95.23	8.53	9.41
NN' dimethylethylenediamine	92.90	9.88	10.64
NNN'N' tetramethylethylenediamine	95.53	12.21	13.38

first end-point was one half of the second. The impurity was found to be of higher molecular weight and may have been NN' diethylethylenediamine.

2. Calorimetric Determinations.

The calorimeter was filled by pipetting 500 ml. of distilled water. The temperature was adjusted to below 25°C. such that upon the addition of the diamine the temperature would be 25°C. A syringe was filled with the diamine, weighed on an analytical balance and at zero time the diamine was added to the calorimeter. The empty syringe was weighed and the amount of diamine dispensed was calculated using the weight of diamine added and the percent titratable amine. Using the heat capacity of the calorimeter and contents, the heat of the solution was found. The values found were lower than the heat of solution of the anhydrous diamines. An arbitrary correction was made which give reasonably accurate values of the heats of solution of the anhydrous diamines, i.e.

$$\Delta H_{\text{anhydrous}} = \frac{\Delta H_{\text{found}}}{(\text{fraction of titratable amine})^2} .$$

The square term was used since the heat of dilution curves are generally parabolic in form so that a square term yields a reasonable first approximation. In the case of NN' dimethylethylenediamine the fraction of amine was not squared due to the presence of the higher molecular weight diamine. In the case of ethylenediamine the heat of solution was found by a different method described later. The results of these determinations appear in Table 15.

The amount of diamine added to the calorimeter was either 0.015 or 0.030 moles. In the former case an excess of acid was used to completely protonate both amino groups, and in the latter case the amount of acid required to protonate only one amino group was used, i.e. about 6 ml. of 4.9117 M hydrochloric acid was used in both cases. Using selected stability constants from the literature, the fraction of each species, i.e. A, AH^+ , and AH_2^{++} , was calculated by a method of approximations before and after the addition of hydrochloric acid. The heat released was corrected for the reaction $H^+ + OH^- \rightarrow H_2O$, the heat of dilution of HCl, and the physical heat of mixing of HCl with the calorimeter contents. From the above data the following expression was set up:

$$\frac{Q}{\text{moles of amine}} = \left[(\alpha_1 + \alpha_2)_{\text{final}} - (\alpha_1 + \alpha_2)_{\text{initial}} \right] \Delta H_1 + \left[(\alpha_2)_{\text{final}} - (\alpha_2)_{\text{initial}} \right] \Delta H_2$$

where Q was the corrected heat released,

α_1 was the fraction of amine in the form AH^+

α_2 was the fraction of amine in the form AH_2^{++} .

By using the results of a pair of runs, the values of the step-wise heats of protonation were calculated by solving simultaneous equations. The results of these determinations are listed in Table 16.

The probable deviation of a single determination of the heat of protonation for the series of diamines was found to be 0.04 kilocalories per mole. On the average this corresponds to 95% confidence limits of 1.08%. Since the

TABLE 16.

THERMODYNAMIC DATA FOR THE STEP-WISE PROTONATION OF DIAMINES,
AT 25°C.

Diamine	$-\Delta F_1$	$-\Delta H_1$	ΔS_1	$-\Delta F_2$	$-\Delta H_2$	ΔS_2	Ref.
	Kilocalories		e.u.	Kilocalories		e.u.	
En*	13.75	12.28	4.93	9.88	10.62	-2.48	29
1,3 Pr	14.53	13.53	3.35	12.12	12.48	-1.21	29
1,4 Bu	14.52	13.83	2.31	12.91	13.37	-1.54	94
1,2 Pr	13.64	12.39	4.19	9.73	10.70	-3.25	95
1,2,2 Mepr	13.64	12.42	4.09	9.26	11.44	-7.31	95
N Meen	14.19	11.48	9.09	10.31	10.49	-0.60	34
NN (Me) ₂ en	13.00	10.63	7.95	9.05	7.51	5.17	96
NN' (Me) ₂ en	13.48	10.52	9.93	9.56	8.68	2.95	97
NNN'N' (Me) ₄ en	12.47	7.50	16.67	8.05	6.91	3.82	97

Recalculated using different stability constants

En	13.90	12.29	5.40	10.15	10.62	-1.58	28
1,3 Pr	14.49	13.64	2.85	12.44	12.38	0.20	98
NN' (Me) ₂ en	14.04	10.41	12.17	10.19	8.70	5.00	34

* Ethylenediamine....En
 1,3 diaminopropane....1,3 Pr
 1,4 diaminobutane....1,4 Bu
 1,2 diaminopropane....1,2 Pr
 1,2 diamino-2-methylpropane....1,2,2 Mepr
 N methylethylenediamine....N Meen
 NN dimethylethylenediamine....NN (Me)₂en
 NN' dimethylethylenediamine....NN' (Me)₂en
 NNN'N' tetramethylethylenediamine....NNN'N' (Me)₄en

runs were done in duplicate, the values in Table 16 should be precise within 95% confidence limits of 0.76%. The error due to errors in the stability constants was not minimized as it was in the case of monoamines and amino acids, so that for a few of the diamines, the stability constants of different workers were used to illustrate the effect on the value of the enthalpy of protonation found. These values also appear in Table 16. The stability constants of Basolo and co-workers appear to be higher than the values reported by others, but this is reasonable since they were determined at an ionic strength of 0.5 whereas the others were determined at a lower ionic strength. In calculating the stability constants of the diamines from the potentiometric titrations, in which no great pains were taken to keep the temperature constant, the values were found to agree better with the lower stability constants reported in the literature.

3. Supplementary Experiments.

It appeared that some specific hydration effects were involved in the solvation of the diamines so a series of supplementary experiments were conducted on selected water-diamine systems in an attempt to elucidate these effects.

a. Heat of dilution curves.

Heat of dilution curves were determined for ethylenediamine, 1,4 diaminobutane, and NNN'N' tetramethylethylenediamine. They were found by injecting about 0.05 moles of the diamine into a metal test-tube which fitted into the cooling tube apperture in the calorimeter lid. The calorimeter was

filled with 500 ml. of water. 0.25 ml. increments of water were added from a syringe. The heat evolved after each increment was added was used in conjunction with heat capacity of the calorimeter and contents to calculate the heat of dilution curves. The resulting curves are shown in Figure 21.

b. Heat of vaporization.

The heat of vaporization of a series of water NNN'N' tetramethylethylenediamine solutions was determined by injecting a weighed amount of the solution into a glass tube packed with steel wool and flash evaporating using a vacuum pump. The tube fitted into the calorimeter, containing 500 ml. of water, through the cooling tube aperture. The apparatus was tested by using water and the heat of vaporization was found, in duplicate, to be 574 calories per gram compared to the literature value 582 calories per gram at 25°C. It was also tested with ethanol and the heat of vaporization found was the same as the literature value, i.e. 240 calories per gram. The results of this study are shown graphically in Figure 22. The solid line represents the heat of vaporization if the two components had vaporized independently.

c. Phase diagrams.

Phase diagrams of water-NNN'N' tetramethylethylenediamine and water-ethylenediamine systems were constructed by examining the cooling curves of the various compositions. The temperature sensing device was a pair of chromelconstantan thermocouples with ice-water being the standard temperature sink. The former system is shown in Figure 23. It was complicated by the fact that the mutual miscibility was decreased

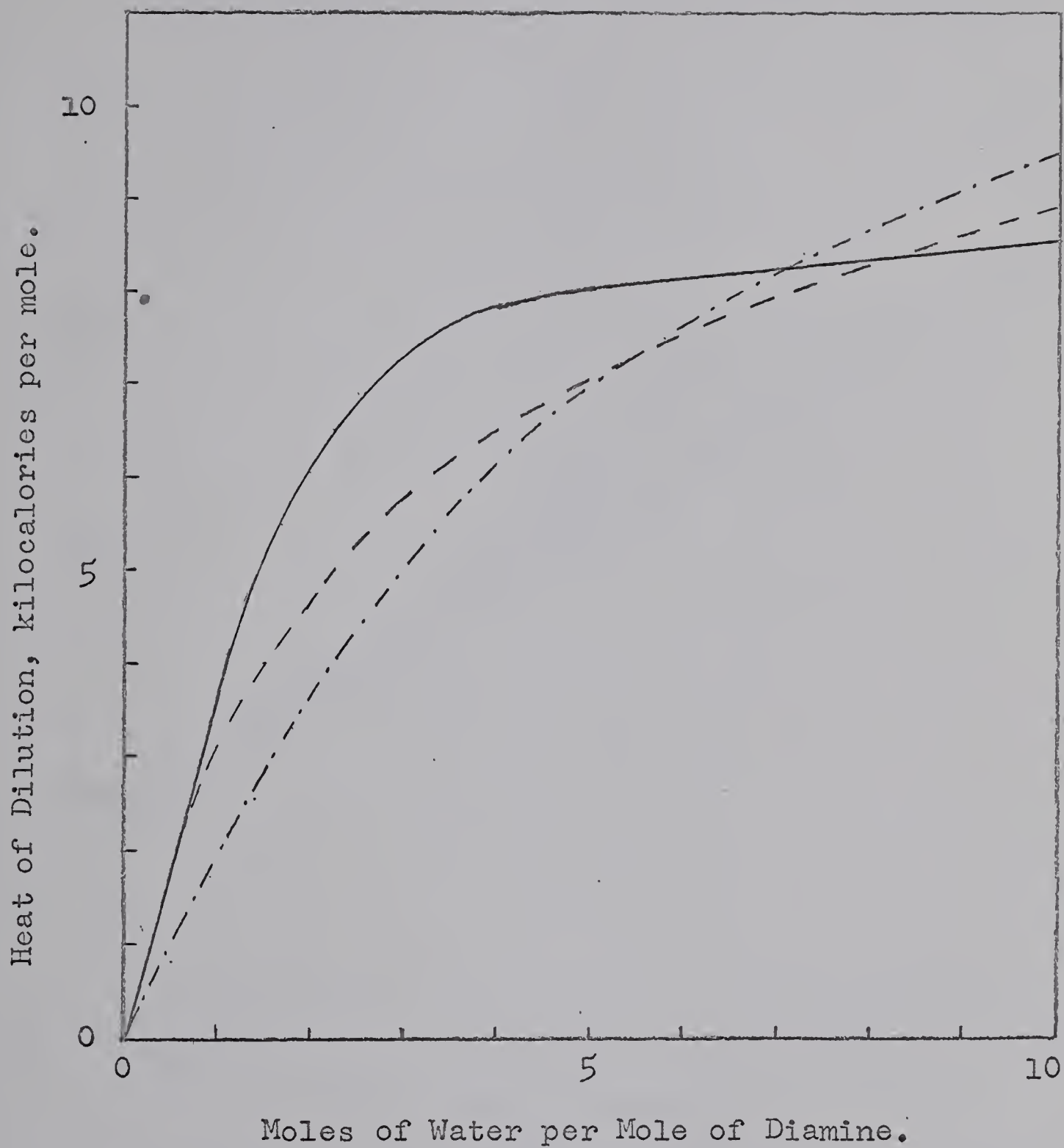


Figure 21. Heat of dilution of diamines.

- ethylenediamine.
- 1,4 diaminobutane.
- · - · - · - · - NNN'N' tetramethylethylenediamine.

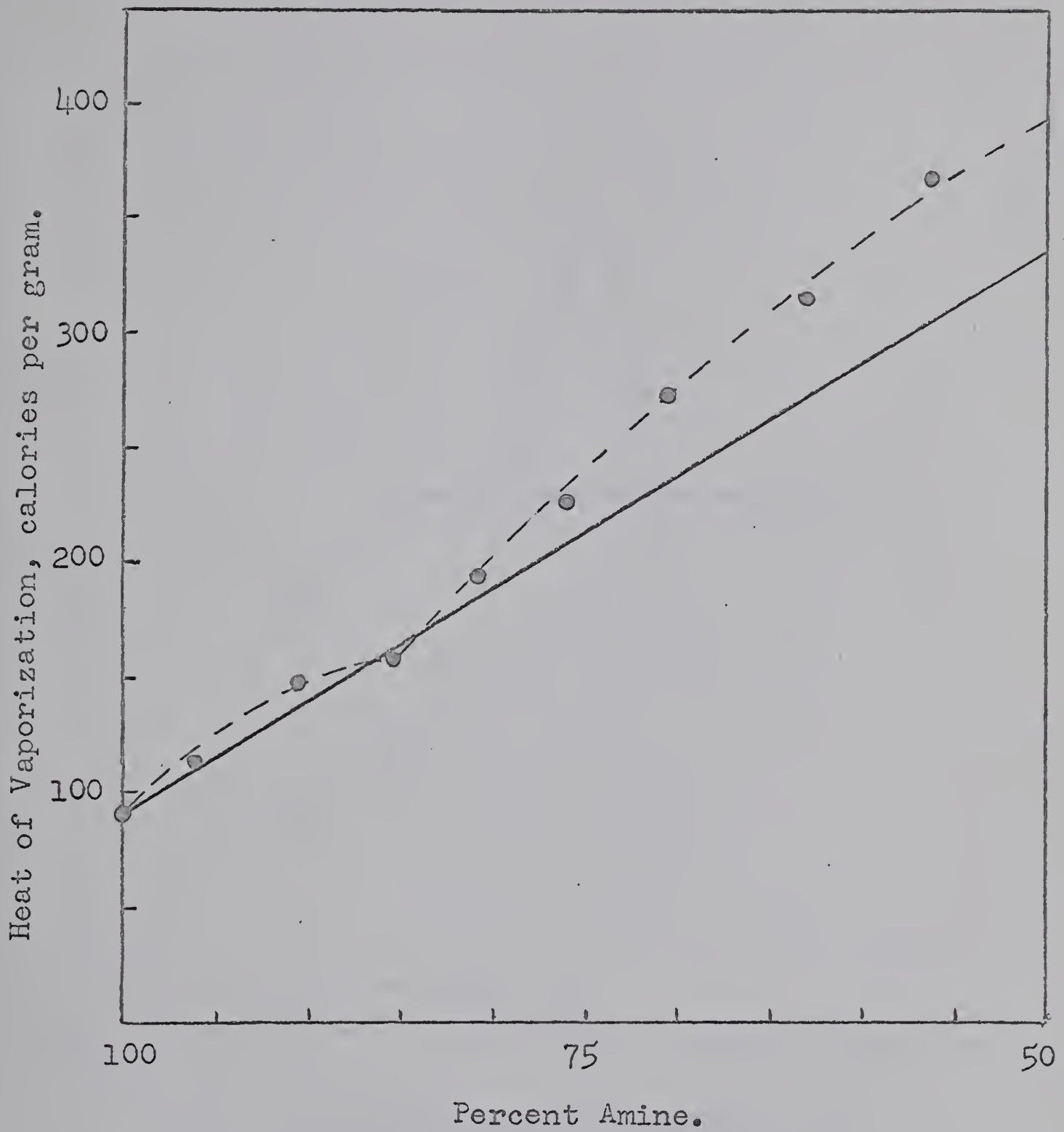


Figure 22 . Heat of vaporization of water - NNN'N' tetramethylethylenediamine solutions.

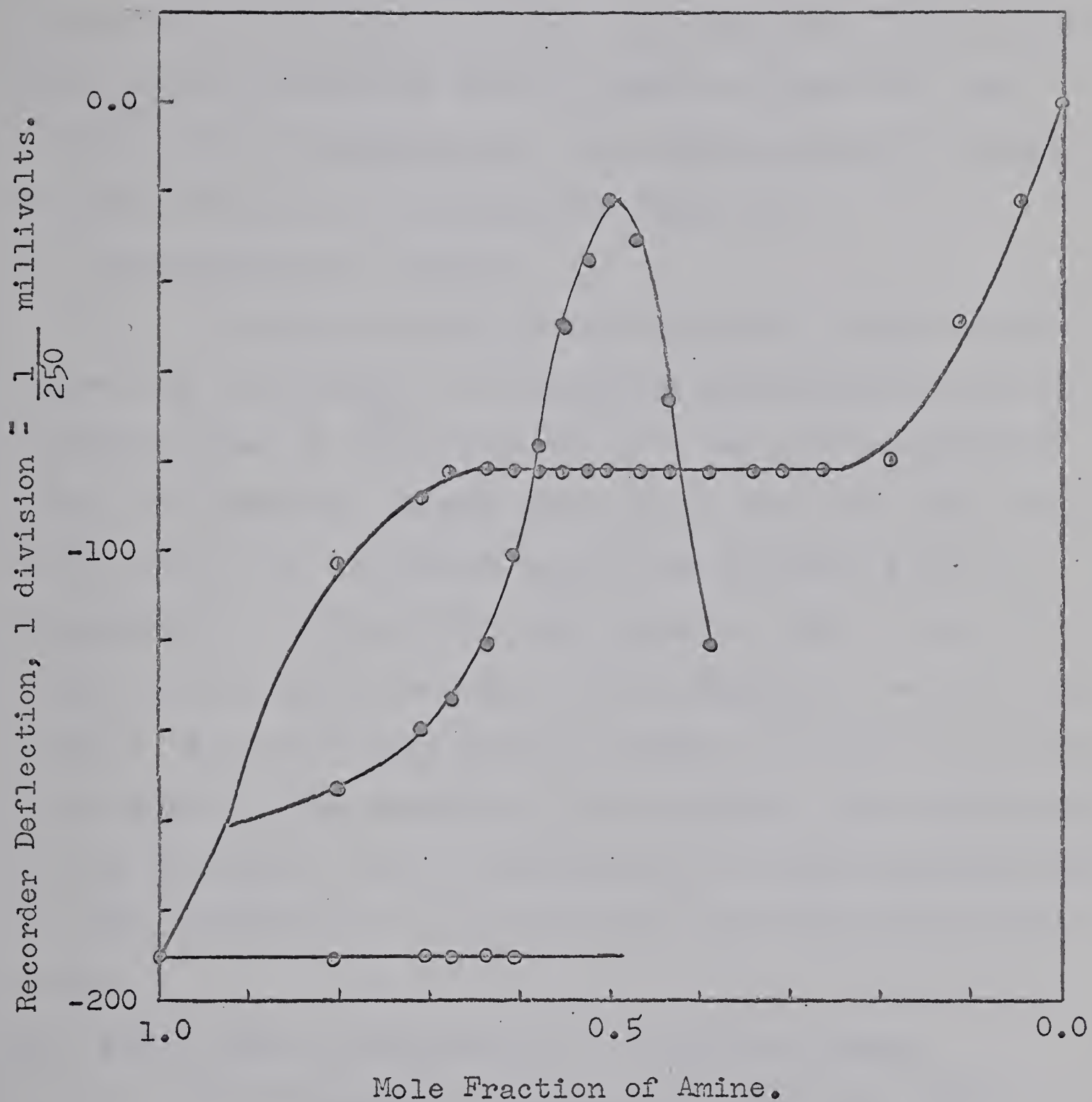


Figure 23 . Phase diagram of water - NNN'N' tetra - methylethylenediamine. Discontinuities in the cooling curves have been plotted.

at lower temperatures so that there were two liquid phases but still there was evidence that a 1 to 1 species did in fact freeze out of the solution. In the latter case, a diagram similar to that of Elgott, shown in Figure 24, was started but not completed for the entire composition range. The portion done was identical to Figure 24.

d. Chromatographic studies.

A series of water-ethylenediamine, water-dipropylamine, and water NNN'N' tetramethylethylenediamine solutions and pure water of various sample size were chromatographed using the apparatus already described. The conditions were: 115°C, 60 ml. of helium per minute and a sample size of 2 microlitres. In Figure 25, the retention time of the water peak has been plotted against the milligrams of water in the sample. As can be seen from the figure, the elution of water was delayed in the presence of the diamines. The differences in the retention time of one milligram of water were ascribed to small differences in the flow-rate and the column temperature.

e. Victor Meyer determination of molecular weight.

No evidence of complexing of water with NNN'N' tetramethylethylenediamine was found in the gas phase at 150°C.

f. Nuclear magnetic resonance studies.

The N.M.R. spectra of a series of water-1,2 diamino-2-methylpropane, water-1,4 diaminobutane, and water-NNN'N' tetramethylethylenediamine solutions were determined. The

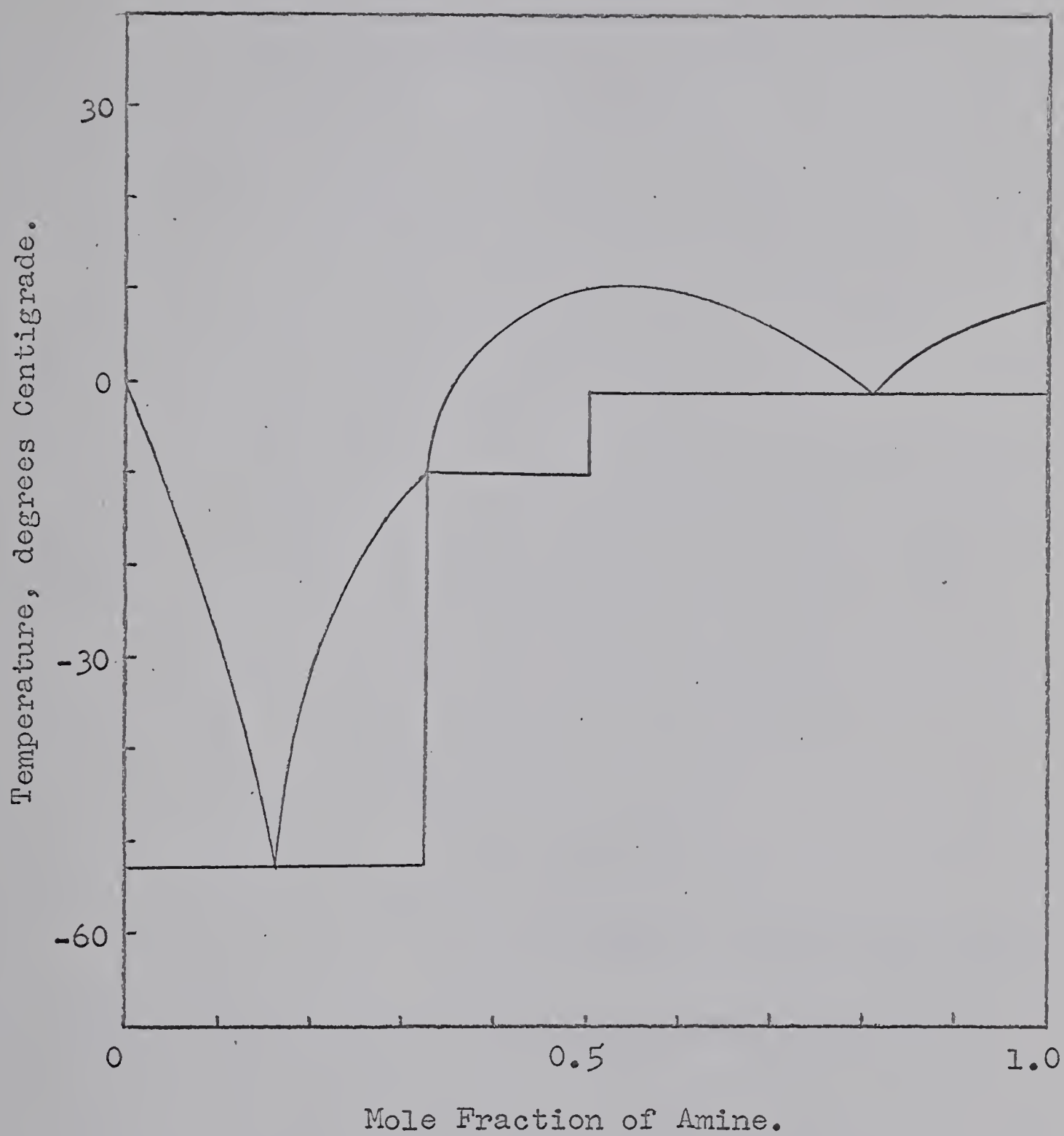


Figure 24. Phase diagram of water - ethylenediamine.
Elgott, J. Russ. Phys. - Chem. Soc., (1929)

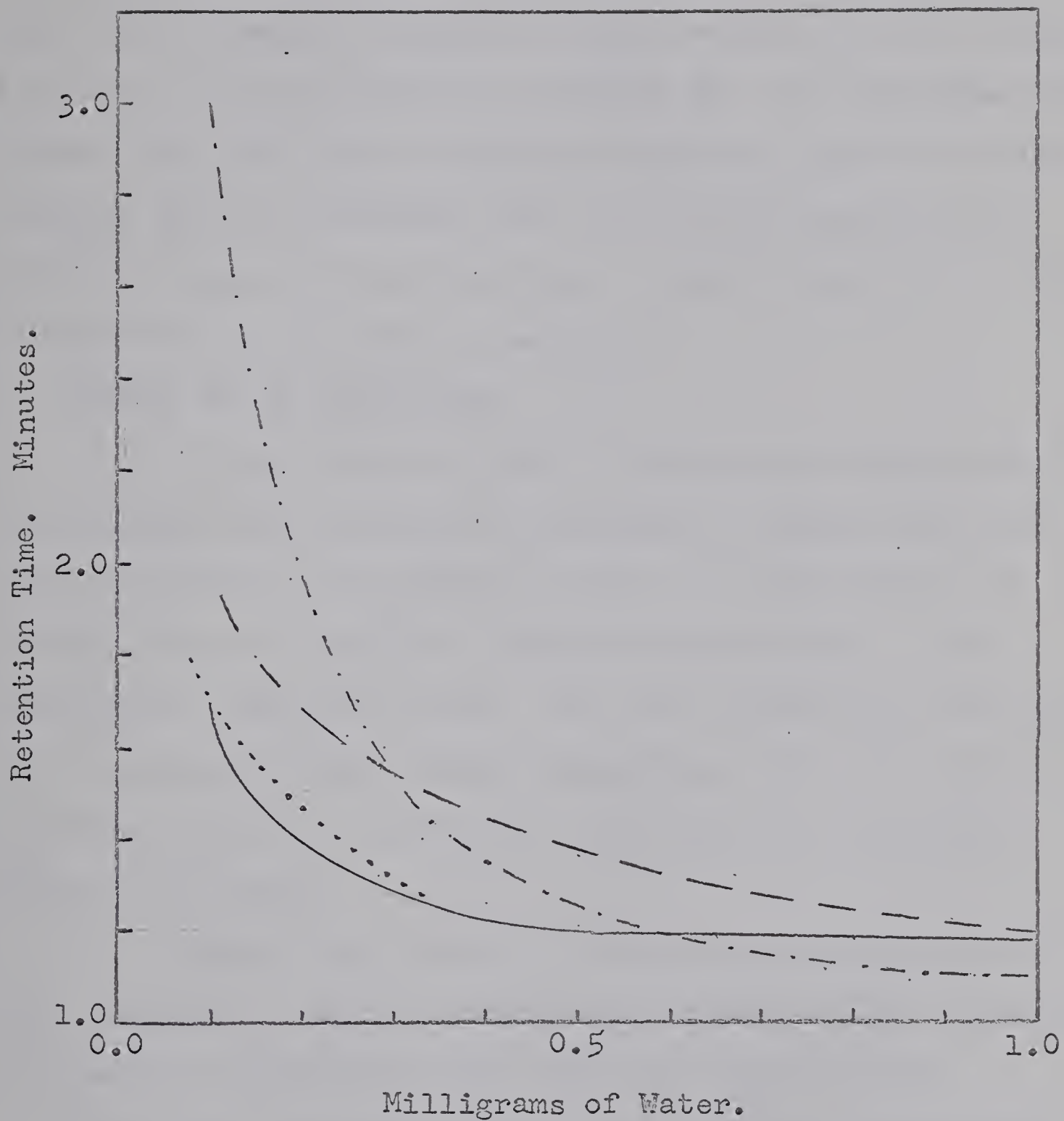


Figure 25. Retention time of water in amine - water solutions.

- water.
- ethylenediamine - water.
- .-.-.- NNN'N' tetramethylethylenediamine - water.
- dipropylamine - water.

chemical shift of the amino proton peak was plotted against the mole fraction of amine. In the first two cases there was found a change of slope at a mole ratio of 1 to 1, amine to water, as is illustrated in Figure 26. In the latter case, however, no such break is readily apparent, but even in this instance when the chemical shift was plotted against the number of moles of amine per mole of water there was noticed a break at 1 to 1, amine to water.

D. ERRORS DUE TO IMPURITIES.

In the determination of the heat of protonation of a particular amino group, the presence of impurities would cause an error in the enthalpy found. In the case of diamines, the error would be directly proportional to the fraction of impurity present. The only impurities which have to be considered were diamine impurities since all calculations were done on the basis of the amount of titratable amine in the sample.

Suppose that some 1,4 diaminobutane was contaminated with 10% of NNN'N' tetramethylethylenediamine. The overall heat of protonation would have been found to be

$$-\Delta H = 0.90 \times 27.20 + 0.10 \times 14.40 = 25.92 \text{ kilocalories/mole.}$$

The error, therefore, would have been 4.7%, which represents the worst possible case.

In the case of NN' dimethylethylenediamine, which had 14.35% of diamine impurities, the probable errors of the step-wise heats of protonation were calculated using the values in the rest of the series. The median value of ΔH_1

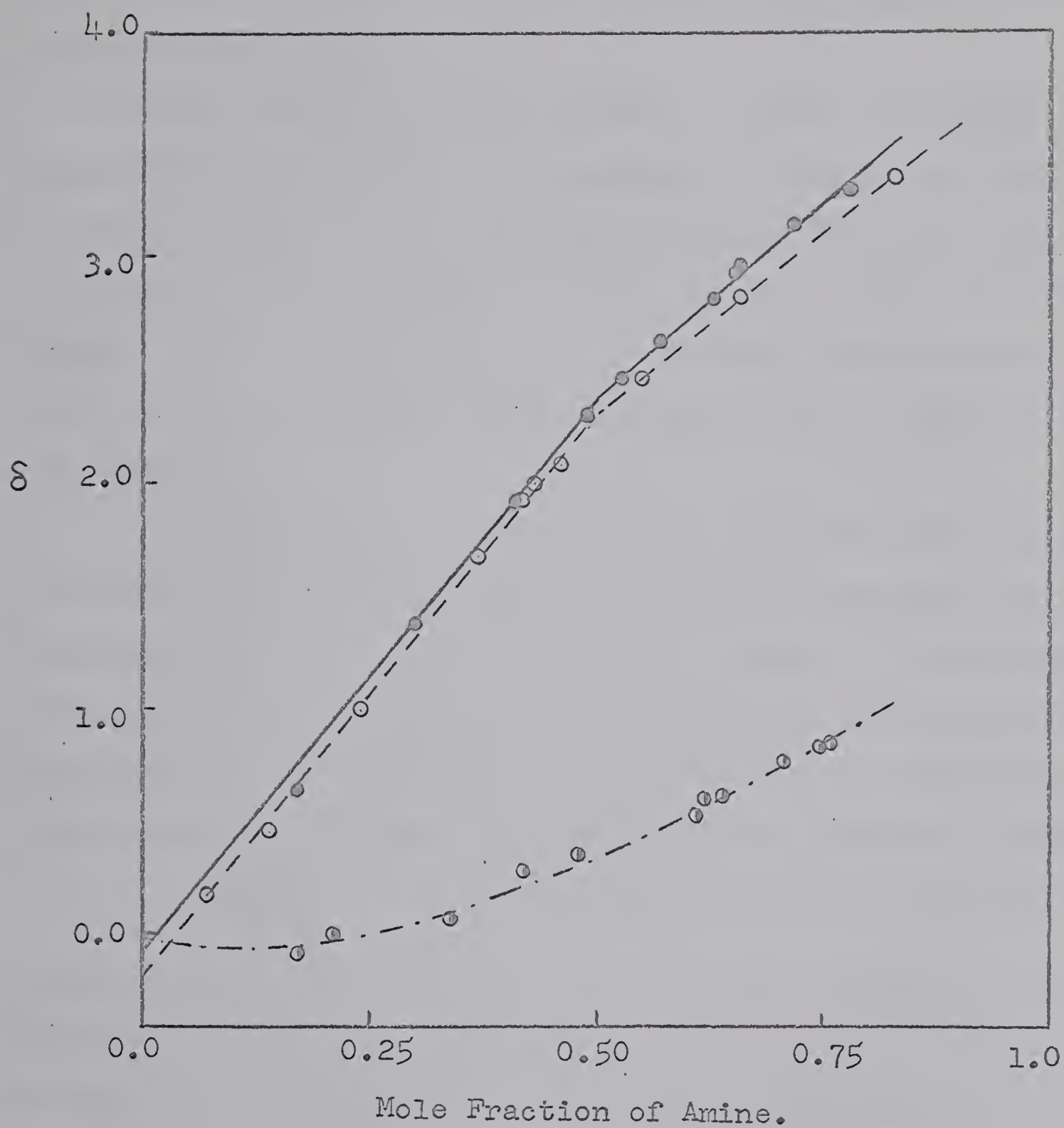


Figure 26 . Amino proton peak shift in water - amine solutions.

- \bullet ——— 1,2 diamino-2-methylpropane - water.
- \circ - - - - 1,4 diaminobutane - water.
- \bullet - . - . - NNN',N' tetramethylethylenediamine - water.

in the series of diamines was 12.28 kilocalories per mole.

The probable error in the heat of protonation of NN' dimethylethylenediamine was

$$(0.8565 \times 10.52 + 0.1435 \times 12.28) - 10.52 = 0.25 \text{ kcal./mole.}$$

The median value of ΔH_2 in the series of diamines was 10.62 kilocalories per mole. The probable error in ΔH_2 was therefore

$$(0.8565 \times 8.68 + 0.1435 \times 10.62) - 8.68 = 0.28 \text{ kcal./mole}$$

Except for the above, the error of the heats of protonation for the diamines in the series considered due to impurities was negligible.

In the case of the monoamines and the amino acids, the error due to impurities was minimized by carrying out the enthalpy determinations in the buffer region. As an extreme case, the system dipropylamine-trimethylamine was considered. The fraction of each amine in the protonated form was calculated at various hydrogen ion concentrations using the formula

$$\alpha = \frac{K[H^+]}{1 + K[H^+]}, \text{ where } \alpha \text{ was the fraction of the amine in}$$

the protonated form and K was the stability constant of the protonated form. The composition of the mixture of the two amines, such that 0.25 of the total amine concentration was protonated, was calculated for a series of hydrogen ion concentrations using the following equation

$$C = \frac{0.25 - \alpha_1}{\alpha - \alpha_1}, \text{ where } C \text{ was the fraction of dipropyl-}$$

amine, α was the fraction of dipropylamine in the protonated form, and α_1 was the fraction of trimethylamine in the protonated form.

Similarly, the composition of the mixture was calculated at a series of different hydrogen ion concentrations such that 0.75 of the total amine concentration was protonated. Various values of hydrogen ion concentration were substituted into the following equation

$$C = \left(0.75 - \frac{K_1 [H^+]}{1 - K_1 [H^+]} \right) \left(\frac{1 + KK_1 [H^+]^2 + (K + K_1) [H^+]}{(K - K_1) [H^+]} \right), \text{ where}$$

K was the stability constant of protonated dipropylamine and K_1 was the stability constant of protonated trimethylamine. C was plotted against the hydrogen ion concentration and then the hydrogen ion concentration was determined from the graph which corresponded to the compositions in the first series. The fraction of the protonated amines were calculated. The heat of protonation of the various compositions were then calculated using the following expression.

$$\Delta H = \frac{(\alpha^1 - \alpha) \times C \times 13.43 + (\alpha_1^1 - \alpha_1)(1 - C) \times 8.91}{(\alpha^1 - \alpha) \times C + (\alpha_1^1 - \alpha_1)(1 - C)}$$

The results of these calculations are shown in Figure 27. It is readily apparent that if the impurity of each amine in the other was less than 10%, the value of ΔH would fall within the experimental 95% confidence limits. In this case there was a factor of 17.4 difference in the stability constants which was quite favourable. It is true that if the difference was smaller that there would be less advantage in working in the buffer region, but by the same token the differences in ΔH would likely be less also, at least in the series considered here.

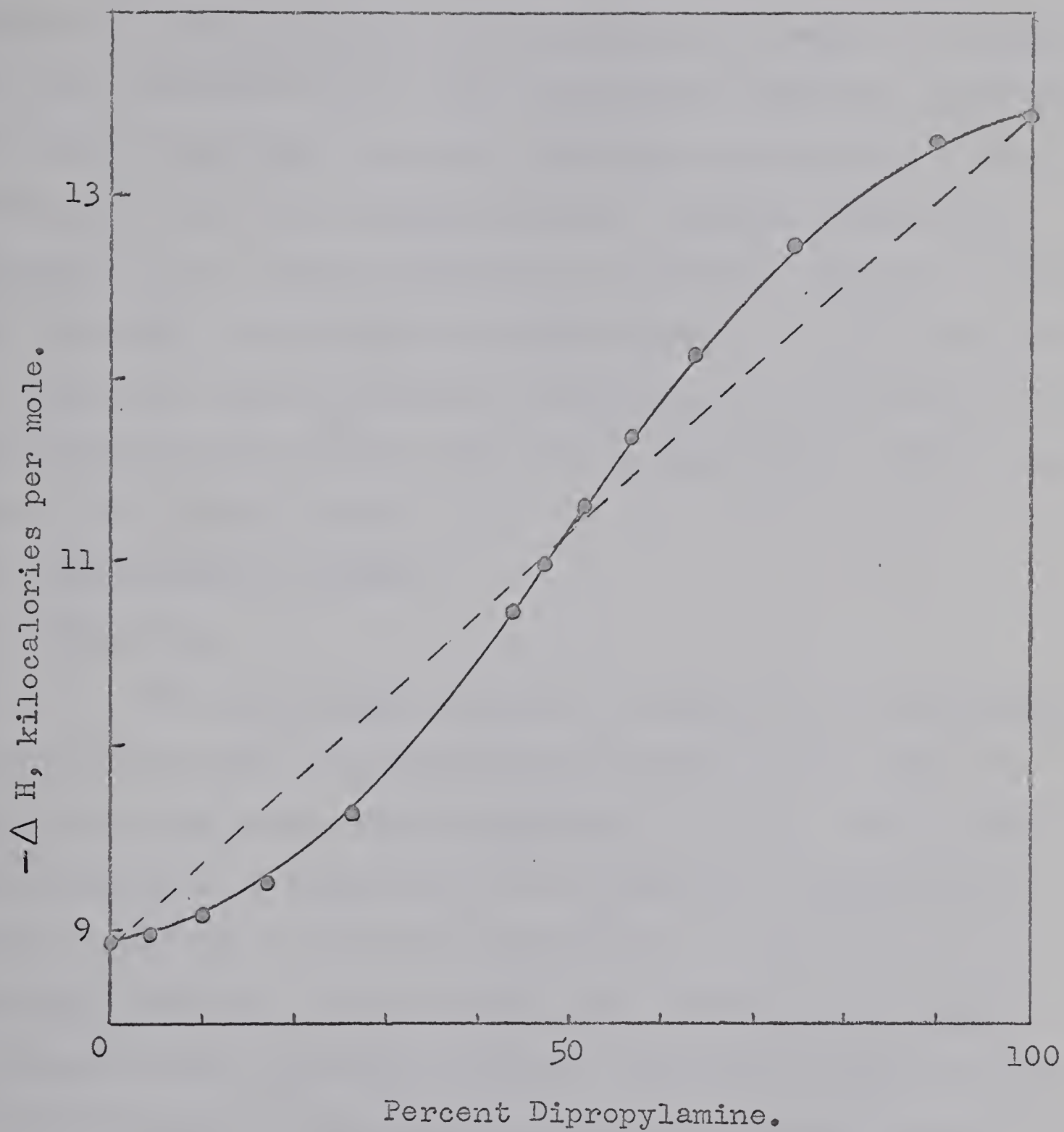


Figure 27 . Heat of protonation which would have been found for various compositions of dipropylamine and trimethylamine.

IV. DISCUSSION

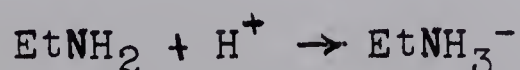
There are many factors which could conceivably affect the thermodynamics of protonation of bases. Of these, the more important factors are substituent effects, including electronic and steric effects, preferred orientation of the molecules, and environmental effects. Certain trends are apparent in the various series of analogous compounds studied and they will be ascribed to these effects. It is convenient to treat the above factors in two groups i.e. solvation effects and non-solvation effects since the environmental effects are due to the solvent water.

A. NON-SOLVATION EFFECTS.

1. Monoamines

In the homologous series of ammonia to n hexylamine, it was found that the protonation reaction became more exothermic as the alkyl chain increased in length. This trend is illustrated in Figure 28. The increasing exothermicity of the reaction is partially explicable in terms of an increasing inductive effect as the chain increases in length. It does not seem probable, however, that there should be any further increase in the exothermicity of protonation due to the inductive effect beyond n propyl or n butyl substitution (99). An attempt will be made to show that the continued increase is probably due to a solvation effect.

The protonation of ethylamine seems to be inordinately exothermic. Although Evans and Hamann (70) found that $-\Delta H$ for the reaction



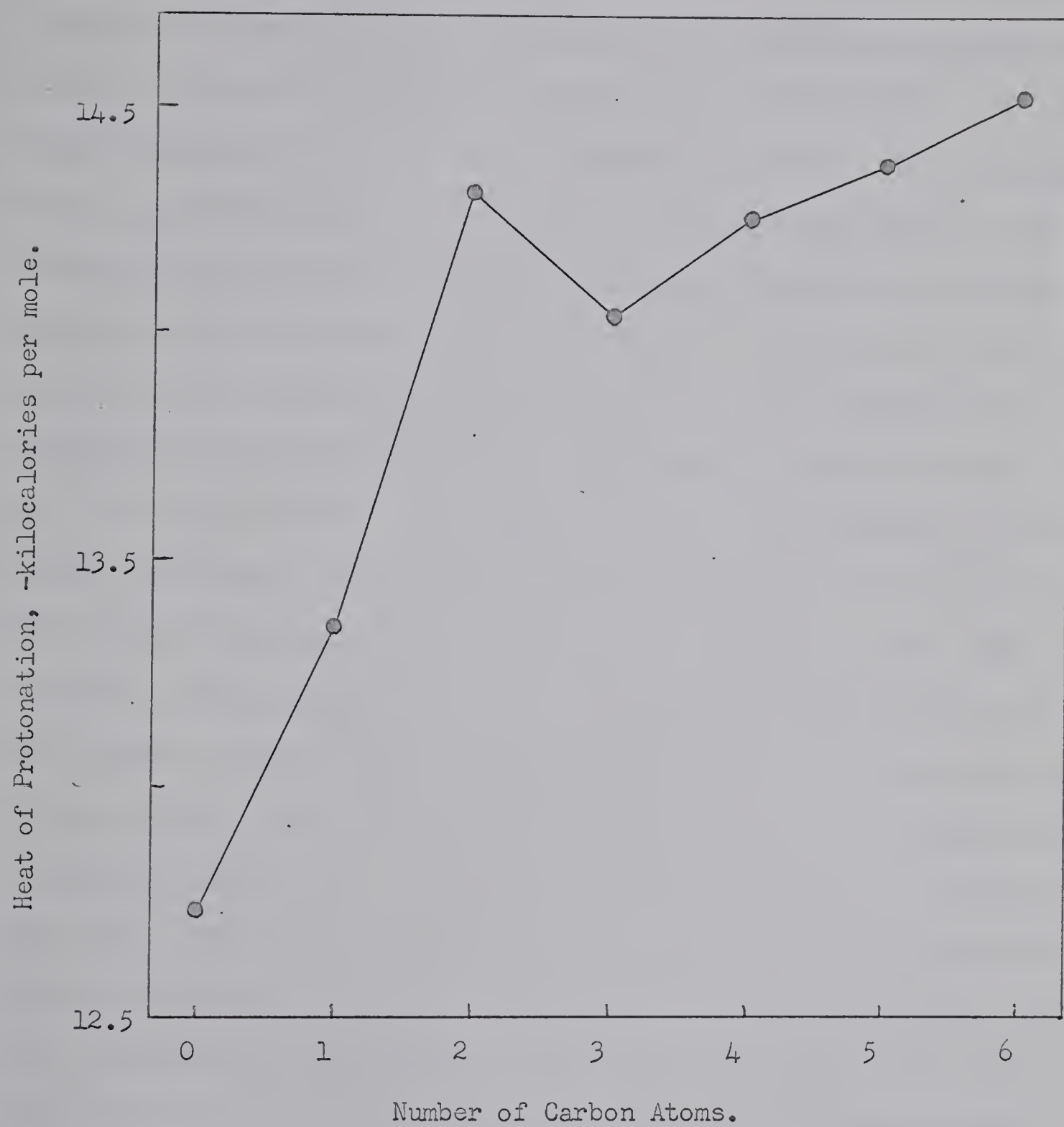


Figure 28. Heat of protonation of n alkyl amines.

was 13.58 kilocalories per mole, the calorimetric result was found to be 14.31 kilocalories per mole. Evans and Hamann's value was determined by extrapolating temperature dependence data to infinite dilution, whereas the calorimetric results were determined at an ionic strength of 0.15. It is unlikely that the difference is due to an ionic strength effect since when the calorimetric results are approximately corrected to infinite dilution (by using the heat of dilution of HCl to infinite dilution) the calorimetric and the temperature dependence results agree within experimental error for the rest of the series (56). In support of the calorimetric results, Forman and Hume (50) found similar behaviour in acetonitrile. This would indicate that the apparent anomaly is not due to a special environmental effect. It could be postulated that in the amines having alkyl groups longer than ethylamine the end of the alkyl chain interferes with the site of protonation thus decreasing the exothermicity of protonation. If this were the case then the protonation of isopropylamine and tertiary butylamine should be significantly more exothermic than the unbranched compounds but this was not found. By way of explanation only a few pertinent facts can be pointed out. Ethylamine hydrochloride has an unusually low melting point (108°C) compared to the rest of the series. If the heats of formation of the series of n alkyl amines are plotted versus the number of carbon atoms in each molecule, it is found that ethylamine does not fall on the smooth curve. If the boiling points^{are plotted} in a similar manner, it is found that

ethylamine exhibits slightly anomalous behaviour. An attempt was made to explain the anomalous behaviour of ethylamine but it was unsuccessful.

In the series methylamine, dimethylamine, trimethylamine, ethylamine, diethylamine, triethylamine, and n propylamine, di n propylamine, there is a steady decrease in the exothermicity of protonation of the amines when one type of alkyl group replaces the amino protons. These trends are illustrated in Figure 29. On the basis of the inductive effect these trends are in the opposite direction to that which would be predicted (100) and must be explained by solvation effects. There is an increase in the exothermicity of protonation in going from methyl to n propyl substitution as would be predicted on the basis of inductive effects but it will be shown to be too large to be explained on this basis alone and is probably partially due to solvation effects.

The fact that the inductive effect does not play a major role in determining the differences in the enthalpies of protonation is illustrated by the differences between the isomers of propylamine and butylamine. It would be expected that isopropylamine would have a greater proton affinity than n propylamine because of the inductive effect (one can consider that they are formed by dimethyl and ethyl substitution, respectively, of alkyl protons of methylamine). All other things being equal, it can be seen that the difference in the inductive effect is small since the increased exothermicity

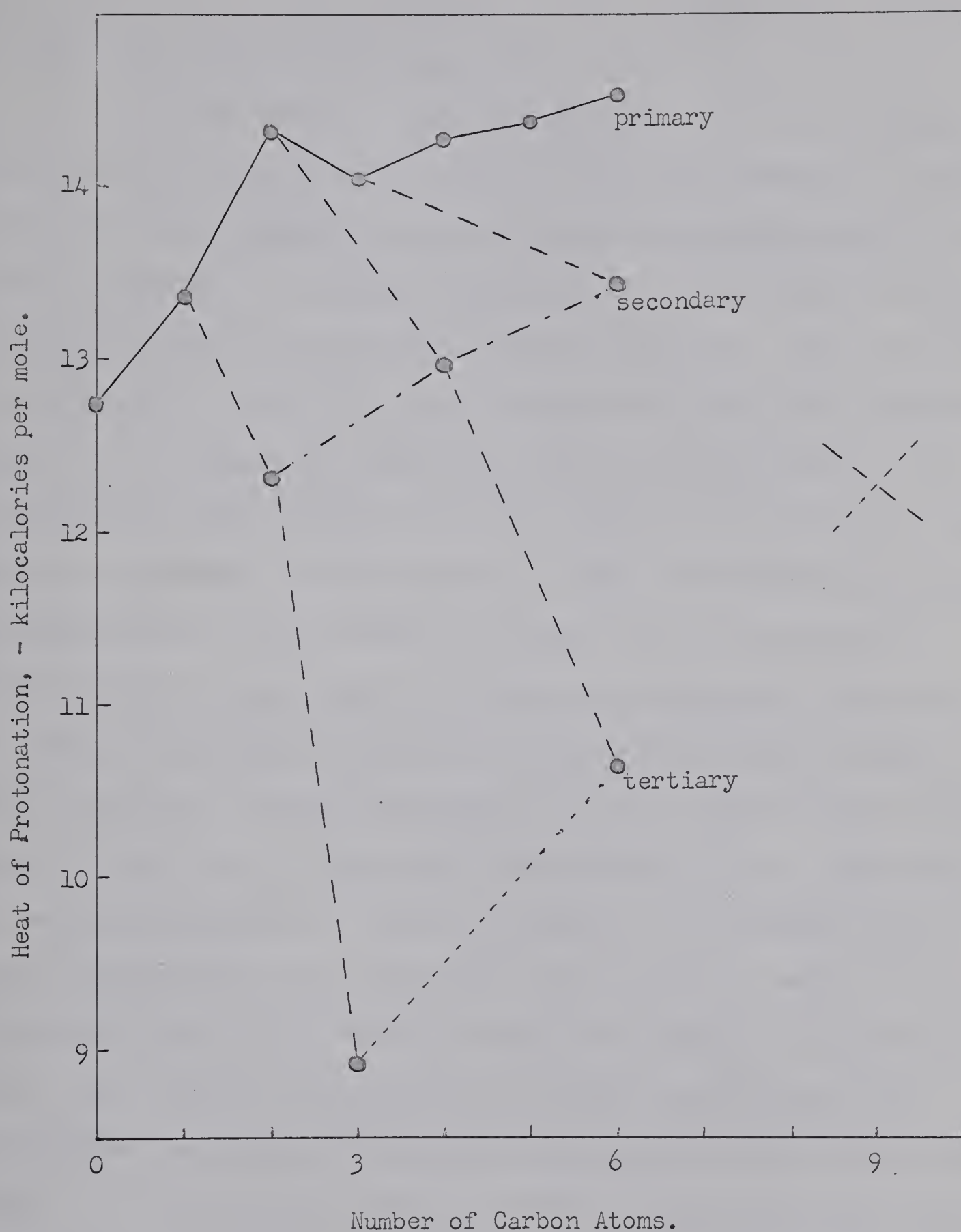
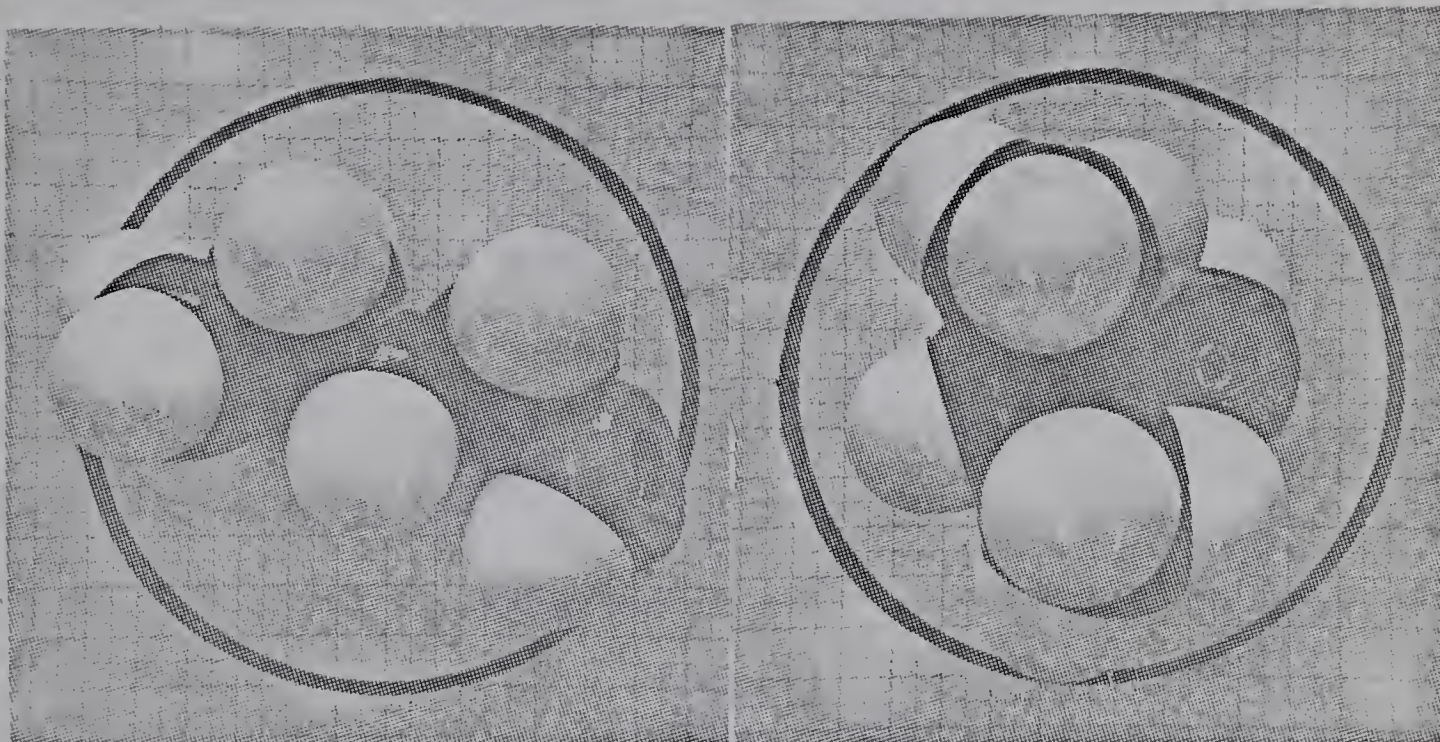


Figure 29. Heat of protonation of primary, secondary and tertiary alkyl amines.

of protonation of isopropylamine over n propylamine amounts to only 0.04 kilocalories per mole.

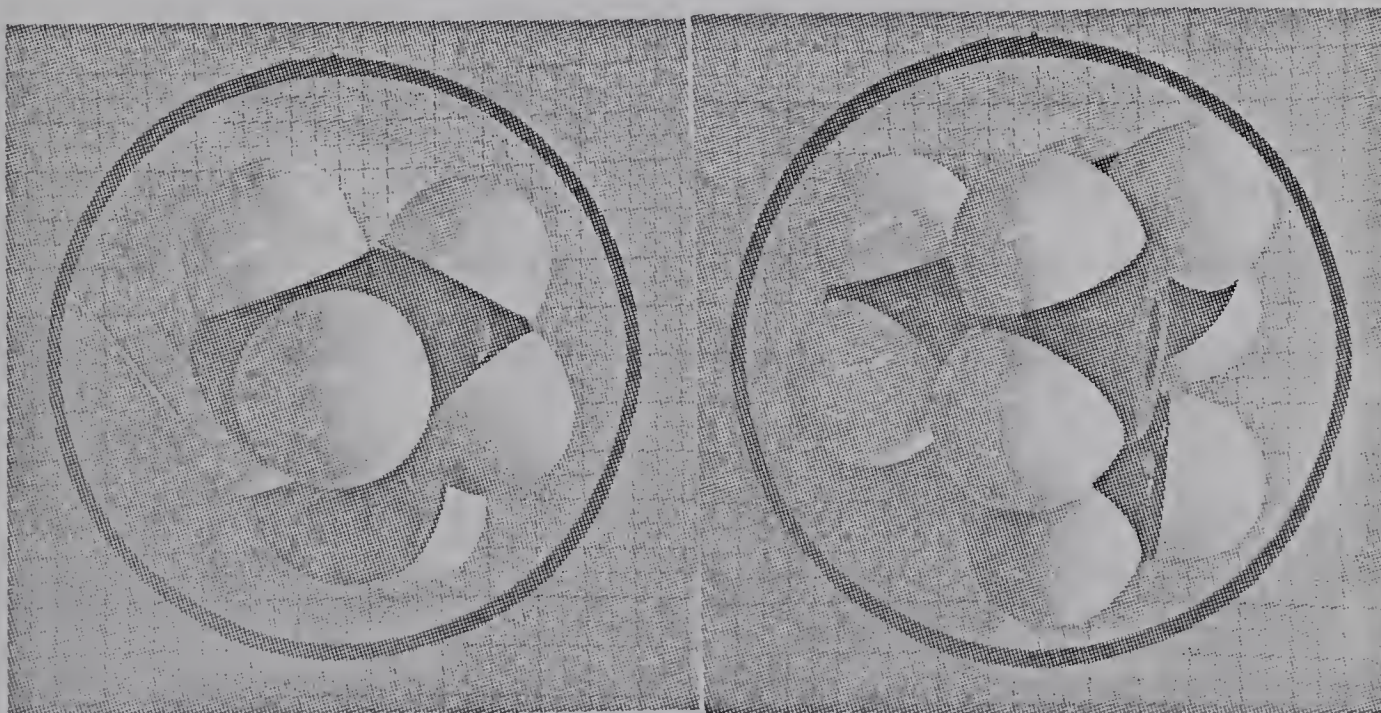
In the case of the butylamines, one would expect on the basis of the inductive effect that the enthalpy of protonation of these isomers would increase in exothermicity in the order of normal butylamine, isobutylamine, secondary butylamine and tertiary butylamine. The values of $-\Delta H$ found were 14.26, 14.10, 14.29 and 14.42 kilocalories per mole, respectively. It is apparent that the differences are small. For isobutylamine the change is in the opposite direction to what would be expected. It is possible that the molecule assumes the orientation illustrated in Figure 30 to a greater or lesser extent in solution. If this were the case, the site of amino protonation would be "protected" by the terminal methyl groups. Similar "protection" to a lesser extent would occur in the case of secondary butylamine but not for normal or tertiary butylamine. One is tempted to speculate that these orientations are induced by the solvent, water, but Forman and Hume (50) found similar differences in acetonitrile, i.e. $-\Delta H$ of protonation of normal butylamine, isobutylamine, secondary butylamine and tertiary butylamine were found to be 25.8, 25.5, 25.8 and 25.9 kilocalories per mole, respectively.

It can be argued that the above effects would be expected to be small since they are differences between isomers, but it was found that the difference between the heat of protonation of benzylamine and methylbenzylamine was only



normal butylamine

iso butylamine



secondary butylamine

tertiary butylamine

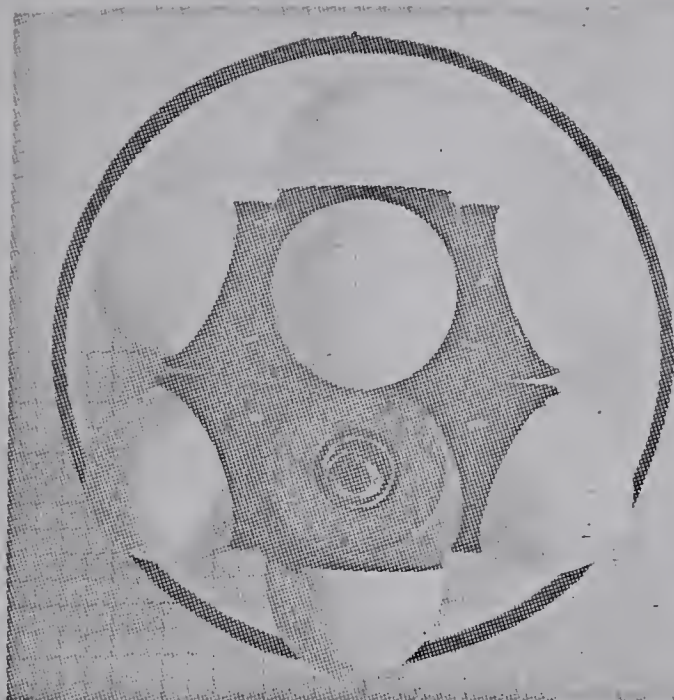
Figure 30. Butylamines.

0.07 kilocalories per mole. It would appear then that inductive effects of alkyl substituents on the alkyl chain play a rather minor role in determining the differences in the enthalpy of protonation and hence the base strength of a given series of amines.

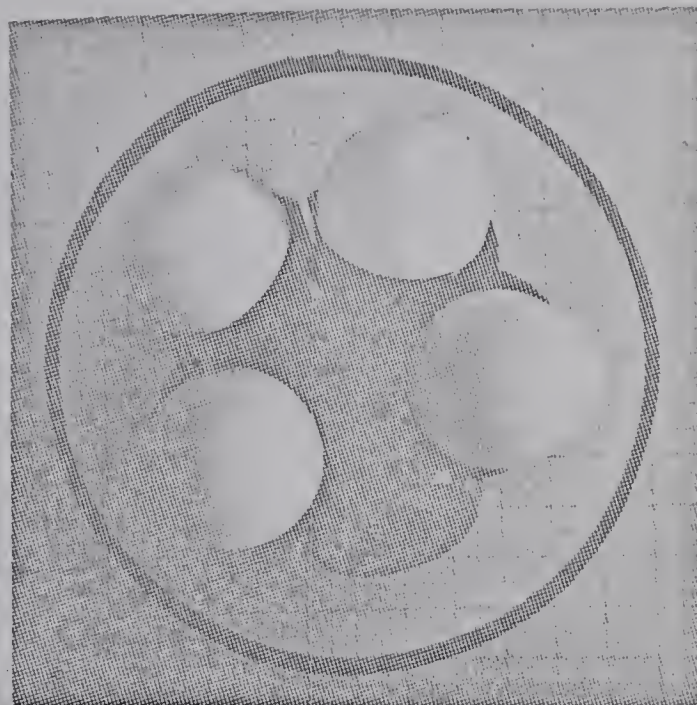
The chain length over which electronic effects persist is indicated by comparing the heats of protonation of the series aniline, benzylamine and phenethylamine which are ~ -5 , -13.12 , and -13.50 , respectively. It would seem that electronic effects would be negligible when the substituent is separated from the amino group by three or four carbon atoms.

The heat of protonation of allylamine was found to be -13.15 kilocalories per mole which is almost identical to the value found for benzylamine (-13.12). This suggests that a double bond has about the same effect on the proton affinity of an amino group as a phenyl group in the same relative position.

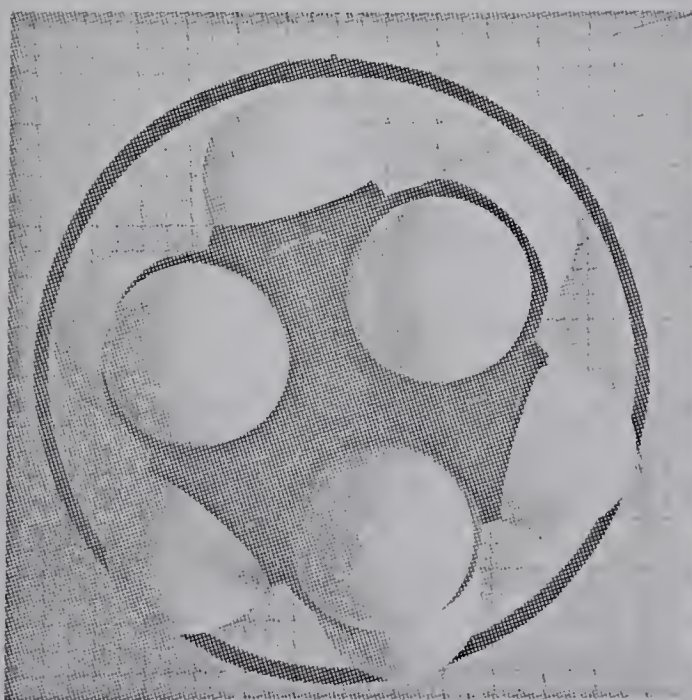
On the basis of the inductive effect it would have been expected that the heat of protonation of piperidine would have been more exothermic than that of pyrrolidine but the values found were -13.07 and -13.50 respectively. An explanation of this apparent anomaly can be given in terms of preferred orientations, i.e. it is likely that the piperidine molecule assumes the boat configuration affording "protection" to the site of protonation whereas pyrrolidine cannot as shown in Figure 31. Upon protonation the piper-



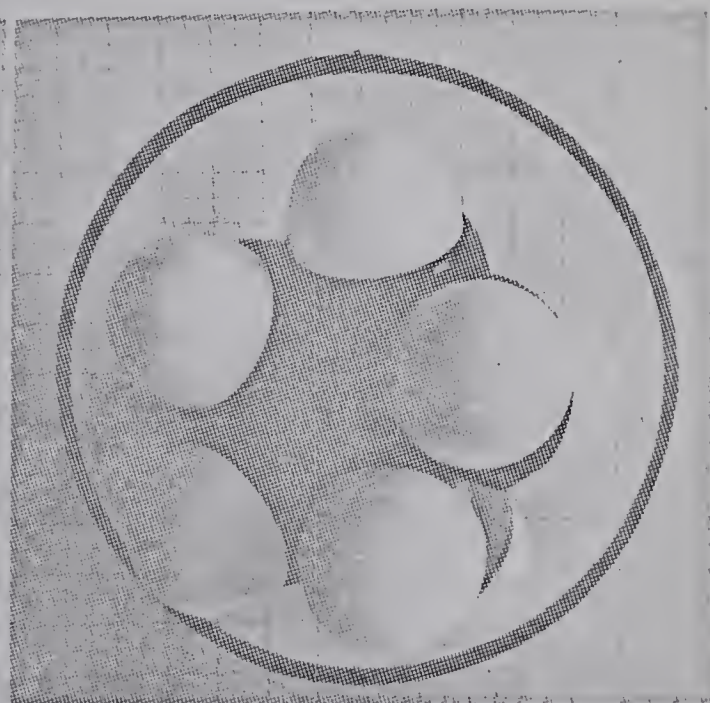
piperidine



pyrrolidine



piperidinium ion



pyrrolidinium ion

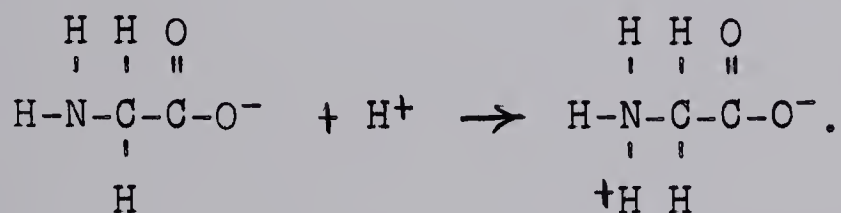
Figure 31. Probable configurations piperidine, pyrrolidine and their ions.

idinium ion formed probably assumes the chair configuration whereas the configuration of pyrrolidine remains relatively constant. This would also account for the difference in entropy of protonation of the two amines, i.e. 7.51 e.u. for piperidine and 6.31 e.u. for pyrrolidine.

2. Amino acids.

a. The amino group.

When the anion of an amino acid is protonated, the proton associates with the amino group to form a zwitterion, e.g.



One of the more important factors affecting the heat of protonation of amino acids is the inductive effect of the carboxylate group. The heats of protonation of the amino acids were found to be about three kilocalories per mole less exothermic than corresponding unbranched alkyl amines, for instance glycine would be α carboxylatomethylamine, alanine would be α carboxylatoethylamine, etc. There was no significant increase in the exothermicity of protonation as there was with the monoamines as the length of the alkyl chain increased. This finding is illustrated in Figure 32 and further suggests that solvation plays an important role in influencing the exothermicity of amino protonation.

As there is an increase in separation of the amino

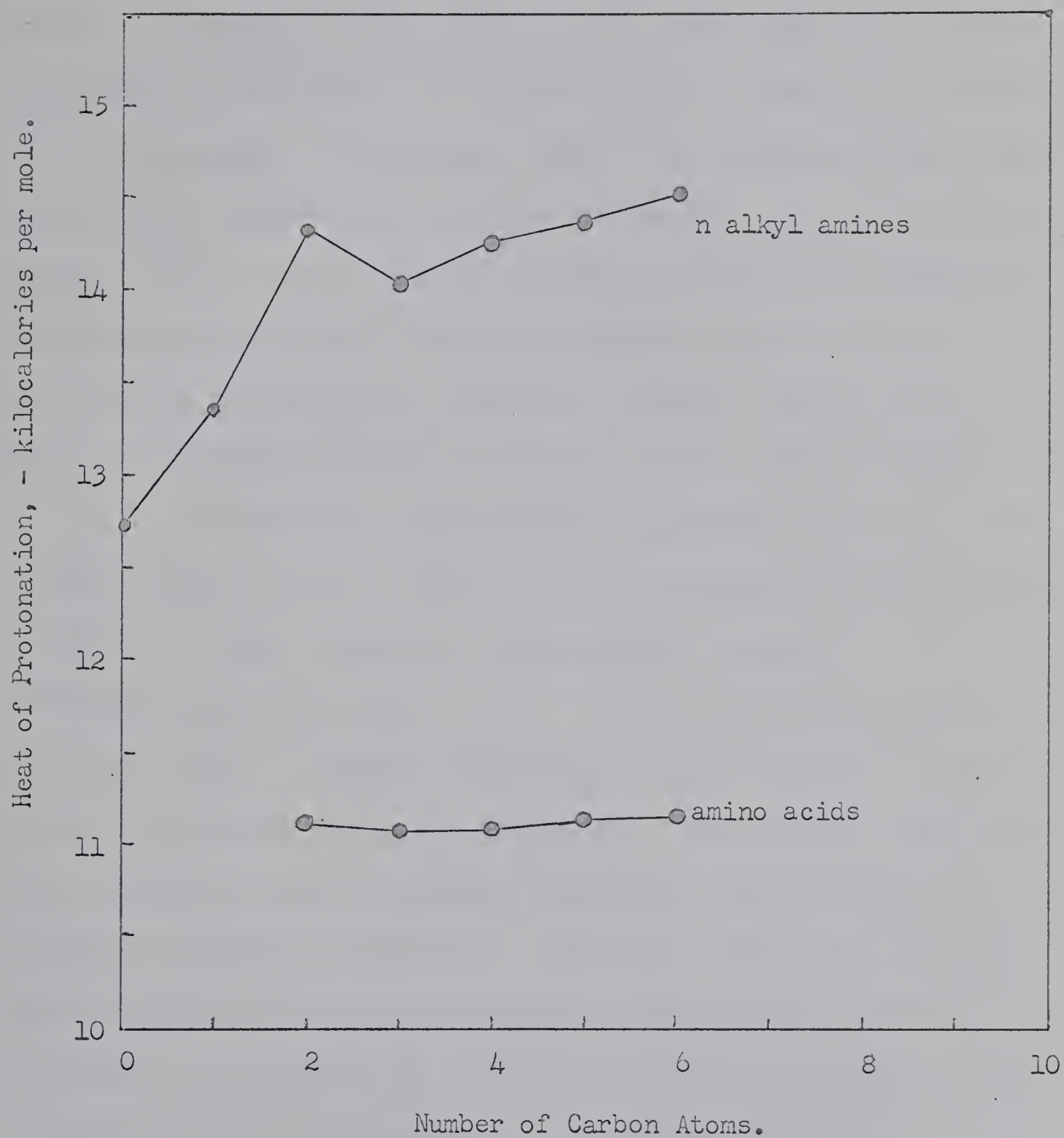
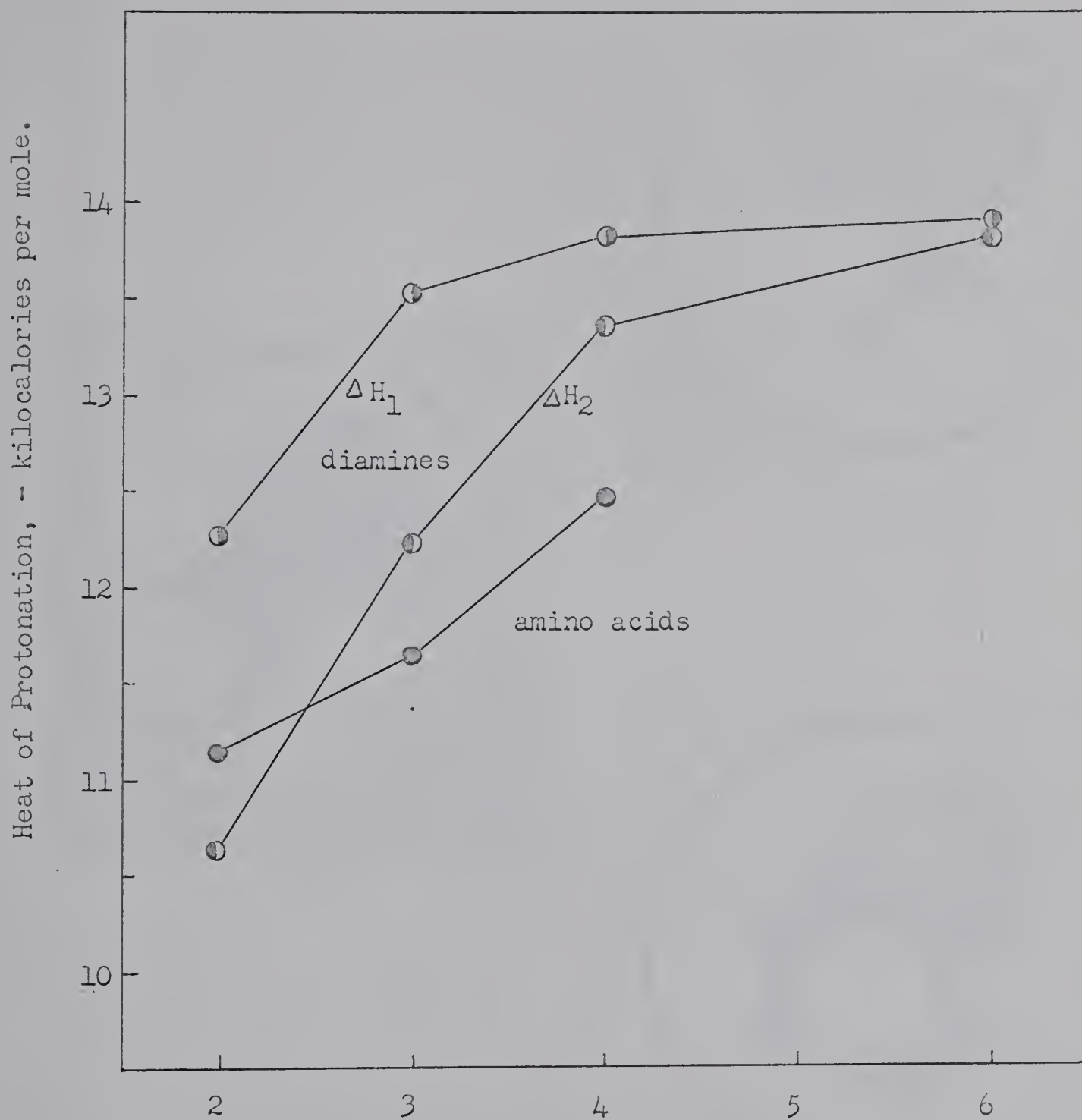


Figure 32. Comparison of the heats of amino protonation of n alkyl amines and amino acids.

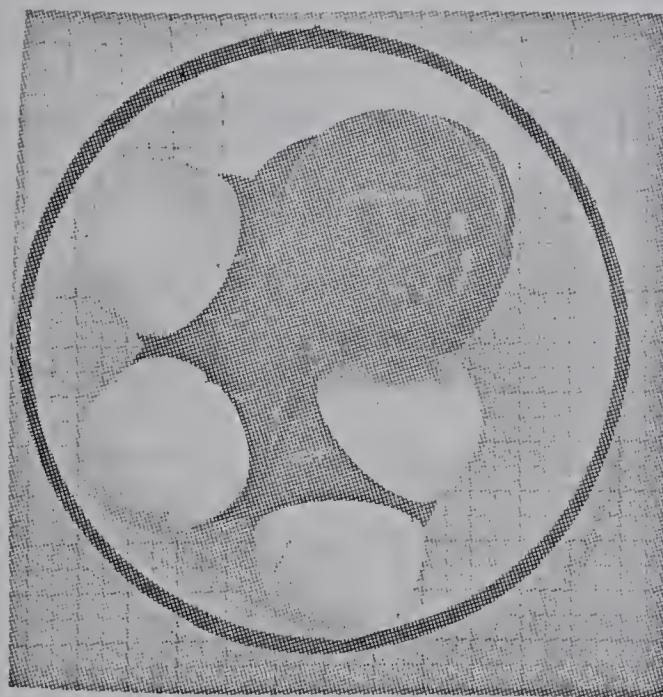
group and the carboxylate group by methylene groups there should be an increase in the exothermicity of the amino protonation because of the reduction of the inductive effect of the carboxylate group. In Figure 33, the heats of protonation of glycine, 3 alanine, and 4 aminobutyric acid have been plotted against the number of carbon atoms in the molecules. On the basis of the inductive effect the greatest difference should have occurred between glycine and 3 alanine where the greatest relative change occurs, but in fact it was found between 3 alanine and 4 amino butyric acid.

It has been shown that in glycine crystals, one of the protons on the amino group is attracted about equally to the two oxygen atoms of the adjacent molecule to form a bifurcated hydrogen bond (7). It is not unreasonable to postulate that a similar phenomenon could occur to some extent intramolecularly in solution. The strain involved in ring formation would probably preclude the existence of intramolecular hydrogen bonding in α amino acids but it could occur in amino acids with greater separation of the functional groups. In Figure 34 the amino acids are shown in the hydrogen bonded configuration. The larger the ring formed the closer the amino proton can approach the two oxygen atoms which can be demonstrated by using molecular models. It can be seen that 4 aminobutyric acid should form the most stable ring structure because of the closer approach of the functional groups and the "staggering" of the alkyl protons (such as in the chair form of cyclohexane) thus decreasing

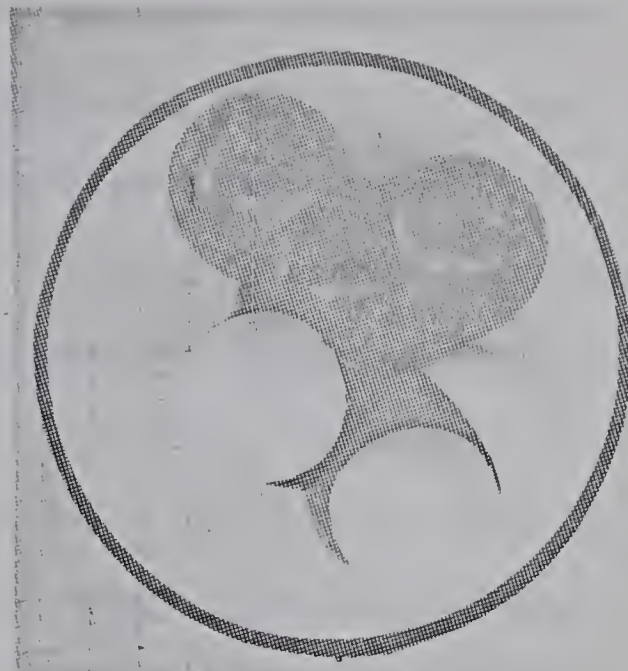


Number of Carbon Atoms Separating the Functional Groups.

Figure 33. The effect on the heats of amino protonation by separation of the functional groups in diamines and amino acids.



3 alanine



glycine



4 aminobutyric acid

Figure 34. Intramolecular hydrogen bonding of amino acids.

the hydrogen - hydrogen repulsion compared to that which would occur in the ring formed by 3 alanine. The argument of ring formation is further strengthened if the heats of protonation of the aminobutyric acids are considered. On the basis of the inductive effect, it would be expected that the heat of protonation of the carboxylate group should become more exothermic in the order 2, 3 and 4 aminobutyric acid. The values found, however, were $-.32$, -0.96 , and -0.58 kilocalories per mole, respectively. Thus if the hydrogen bond formed in the case of 4 aminobutyric acid is indeed stronger (and thus involves a more exothermic heat of formation) than 2 and 3 aminobutyric acid, the same extra enthalpy change will be involved in the protonation of the amino and the carboxylate groups. The effect will be that the protonation of the amino group will be more exothermic and the protonation of the carboxylate group will be less exothermic than would have been expected in the absence of intramolecular hydrogen bonding.

In addition to the enthalpy changes, the entropy changes are consistent with the hypothesis of intramolecularly hydrogen bonded ring formation in the aminobutyric acids. The entropy of protonation of the amino group was found to decrease in the same order which is exactly what would be expected if ring formation occurred simultaneously with carboxylate protonation, i.e. due to a loss and a gain, respectively, in rotational entropy.

In the series glycine, sarcosine and NN dimethyl-

glycine, the heat of protonation of the amino group became less exothermic as methyl substitution took place on the nitrogen atom. The trend was very similar to that found for the series of methylamines. Again the change cannot be explained in terms of any effect other than solvation effects.

The effect of phenyl, hydroxy and mercapto substitution on the terminal methyl group of 2 alanine was examined. The $-\Delta H$ values of protonation of the amino group of phenylalanine, serine, and cysteine were found to be 10.93, 10.58, and 8.48 kilocalories per mole, respectively.

The heat of protonation of the amino group of valine seems slightly low, but it can be rationalized in a similar manner to the case of isobutylamine, i.e. the site of protonation is "protected" by the terminal methyl groups.

The case of 2 methylalanine appears to be similar to that of tertiary butylamine, i.e. the inductive effect is important giving rise to an increased exothermicity of amino protonation.

b. The carboxylate group.

As has been suggested earlier the heat of protonation of the carboxylate group not only depends on inductive effects but on the formation of rings due to intramolecular hydrogen bonding. In the case of the α amino acids, as substitution occurs on the alkyl carbon and on the amino group there was found a general decrease in the exothermicity of the heat of protonation of the carboxylate group. This trend is opposite to what would be expected on the basis of

the inductive effect but is explicable in terms of solvation effects.

3. Diamines.

In diamines, the two amino groups exert an inductive effect on each other, i.e. they will tend to mutually decrease the proton affinity of each other and when the first amino group has been protonated the ammonium group formed will exhibit an enhanced effect to decrease the proton affinity of the second amino group. Thus the heat of protonation of the first amino group should be less exothermic than a similar monoamine and the heat of protonation of the second amino group should be still less exothermic. This was, in fact, found to be the case in the diamines studied.

As the amino groups are separated by more carbon atoms, the above effect should be diminished. In Figure 33 are plotted the values of ΔH_1 and ΔH_2 versus the number of carbon atoms separating the amino groups. In addition to the enthalpy data found in this work for ethylenediamine, 1,3 diaminopropane and 1,4 diaminobutane, the enthalpy data of Everett and Pinsent (27) for 1,6 diaminoheptane are included. It can be seen that the inductive effect decreases rapidly as separation of the amino groups is increased.

In the series ethylenediamine, 1,2 diaminopropane and 1,2 diamino-2-methylpropane, it was found that the heats of protonation of the first amino group were very similar, i.e. the values of $-\Delta H_1$ were 12.28, 12.39 and 12.42 kilocalories per mole, respectively. On the other hand, the

$-\Delta H_2$ values showed a greater variation, i.e. 10.62, 10.70 and 11.44 kilocalories per mole, respectively. It is interesting to note that the free energy changes were in the opposite direction so that the entropy changes became less positive as shown in Table 16. The loss in entropy (or at least the smaller gain) would be expected as the diamines added a second proton since there would tend to be a loss in rotational entropy due to the repulsion of the two positive charges. That the greatest increase in exothermicity should be involved in the protonation of the second amino group was not expected, however, as the first proton should be added to the amino group nearest to the site of alkyl substitution and consequently should exhibit the largest enthalpy change in view of the inductive effect.

Two series arise from the N methyl substitution of ethylenediamine, i.e. the symmetrical methyl substitution and the unsymmetrical methyl substitution. In the first series are ethylenediamine, NN' dimethylethylenediamine and NNN'N' tetramethylethylenediamine and in the second series are ethylenediamine, N methylethylenediamine and NN dimethylethylenediamine. Again, as can be seen from Table 16 and Figure 35, there is a general trend towards less exothermic heats of protonation as the amino groups go from primary to secondary to tertiary. This trend can be explained in terms of solvation.

4. Comparisons.

It is of interest to compare similar series within

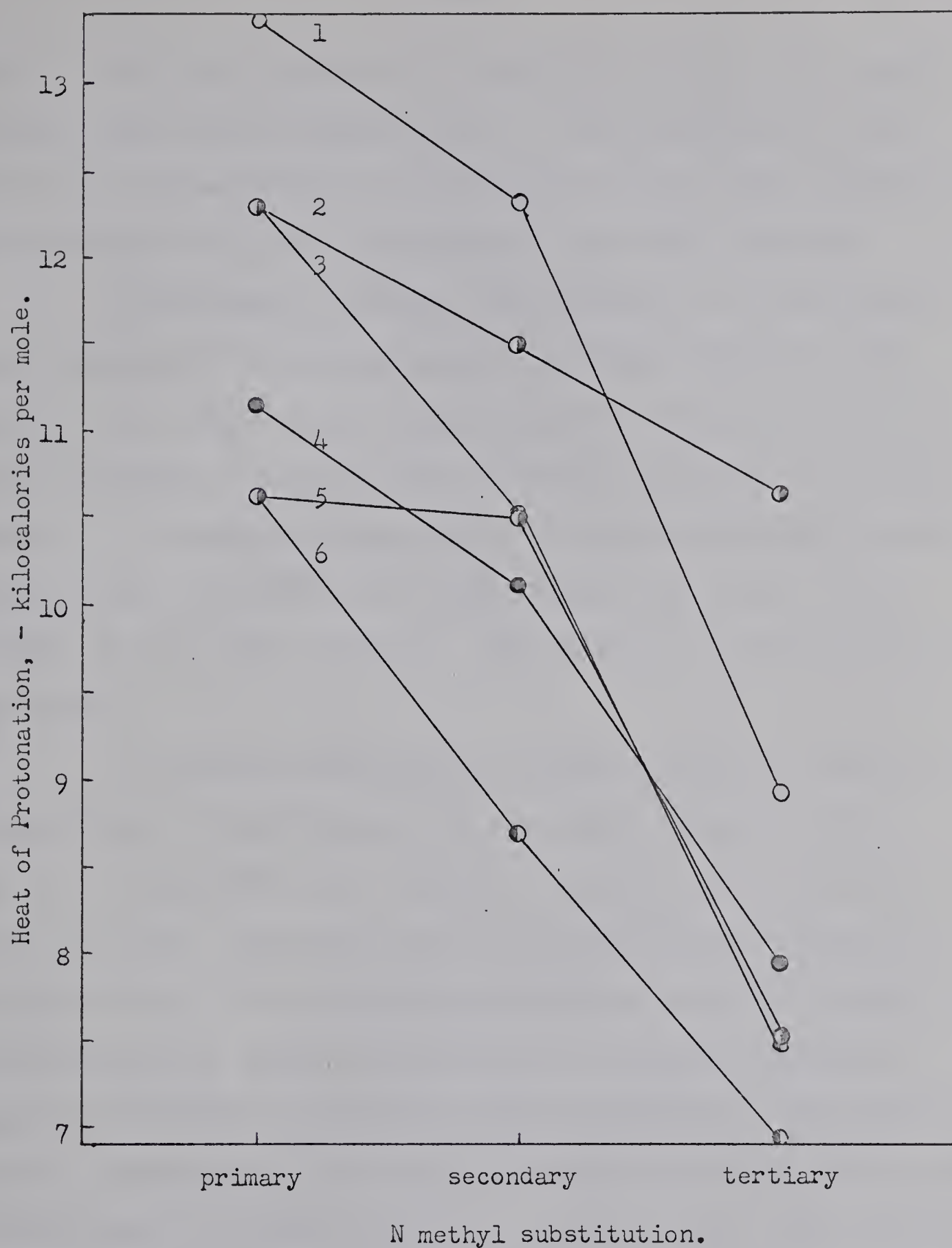


Figure 35. Heat of protonation of primary, secondary and tertiary amino groups.

1. methylamines
2. ethylenediamines, unsymmetrical methyl substitution, ΔH_1
3. ethylenediamines, symmetrical methyl substitution, ΔH_1
4. glycines
5. ethylenediamines, unsymmetrical methyl substitution, ΔH_2
6. ethylenediamines, symmetrical methyl substitution, ΔH_2

each of the three classes of compounds studied, i.e. monoamines, amino acids and diamines. The similarity of the effect on the enthalpy of protonation of the amino group by various modes of alkyl substitution is very striking.

The effect of methyl substitution on the carbon atom adjacent to the amino group in three series of compounds, i.e. ethylamine, isopropylamine and tertiary butylamine; glycine, 2 alanine and 2 methyl-2-alanine; ethylenediamine, 1,2 diaminopropane and 1,2 diamino-2-methylpropane, examined and the effect of substitution was found to be similar in all three series. The effect is illustrated in Figure 36.

N methyl substitution produced similar trends in the enthalpy of protonation of the amino group of four series of compounds, i.e. methyl, dimethyl and trimethylamine; glycine, sarcosine and NN dimethylethylenediamine; ethylenediamine, N methylethylenediamine and NN dimethylethylenediamine; ethylenediamine, NN' dimethylethylenediamine and NNN'N' tetramethylethylenediamine, the last two series' representing the unsymmetrical and symmetrical methyl substitution of ethylenediamine, respectively. The similarity of these trends is illustrated in Figure 35.

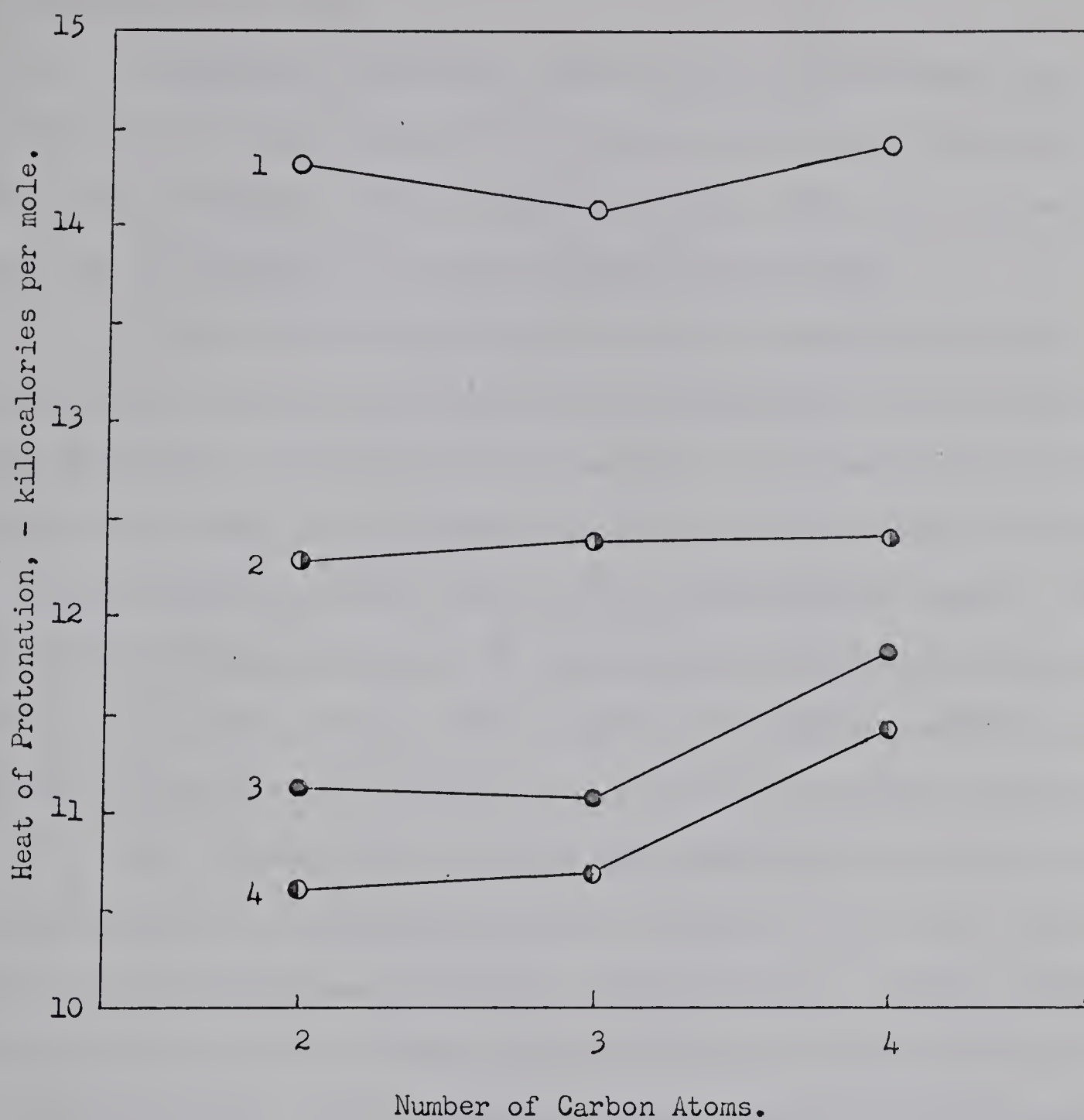


Figure 36. The effect on the heats of amino protonation by methyl substitution on the α carbon atom.

1. monoamines
2. ethylenediamines, ΔH_1
3. glycines
4. ethylenediamines, ΔH_2

B. Solvation Effects.

Whenever a reaction takes place in solution, the interaction of the solvent with the reactants and the products must be considered. This is particularly true of a solvent that has a tendency to form discrete structures.

The unique properties of liquid water have been attributed to the association of its molecules by hydrogen bond formation. The ability of water to assume polymolecular structured forms is enhanced by the fact that the bond angle in liquid water is very close to the tetrahedral angle. The propensity of liquid water to form intermolecular hydrogen bonds is the main reason that water has a higher melting point, boiling point and dielectric constant than related compounds (101). That liquid water is largely associated is shown by the enthalpies of sublimation and fusion of ice, i.e. 12.2 and 1.44 kilocalories per mole, respectively. Of the enthalpy of sublimation, only about one fifth can be attributed to van der Waals forces (101), therefore the energy of each hydrogen bond must be about 5 kilocalories per mole in ice. The enthalpy of fusion shows that only about 15% of the hydrogen bonds of ice are broken upon melting.

In recent years there has been widespread concurrence with Frank's view (64) that the association of liquid water leads to "flickering" structures made up of many water molecules. The nature of these structures is not at all certain at the present. They have been viewed as compact "iceberg-like" clusters (102) and as networks of cages, either essentially

filled with unbonded water molecules (7) or vacant to a large extent (103, 104, 105). Recently an experimental argument in favour of the network model without many vacancies has been published (73).

If a foreign body is introduced into liquid water there must be structural dislocations so that the intruder can be accommodated. The simplest case would be the replacement of a water molecule in the solvent structure by a solute particle. This ideal case is not even approximately attained by closely related compounds, e.g. hydrofluoric acid, ammonia and hydrogen sulfide, so that generally speaking the solute molecule must be accommodated by some process other than simple replacement.

As has been indicated in the previous section, the magnitude of the differences of the enthalpy of amino protonation of various compounds studied are only partially explicable in terms of non-solvation effects. The differences can, however, be rationalized in terms of solvation effects.

In the reaction:

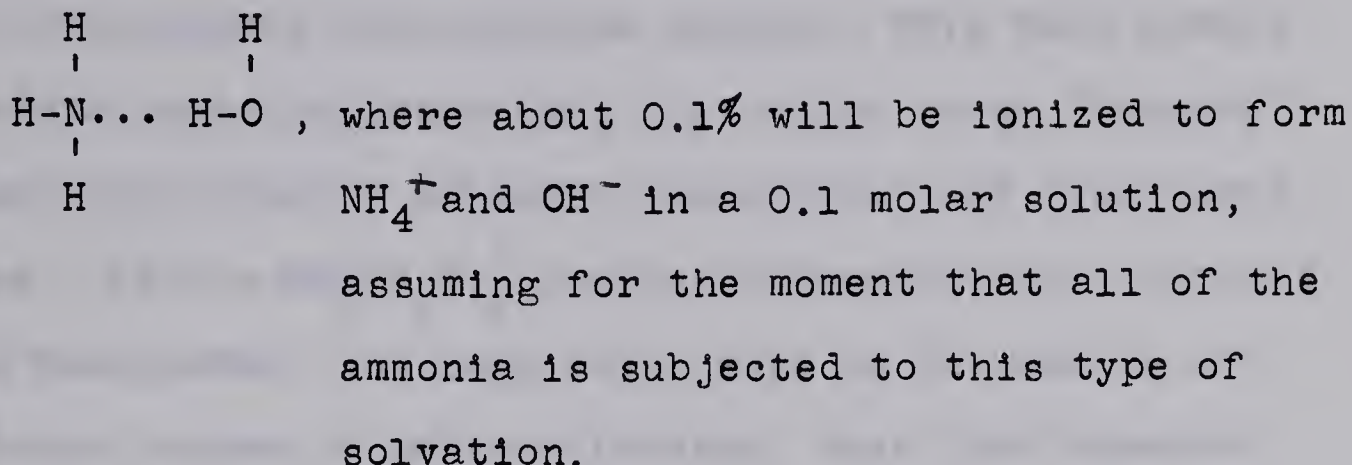


where A represents an amine, any difference in the enthalpy of protonation due to solvation effects for a series of amines should be due to differences in solvation of the amine molecules and the amino cations formed, since solvation effects due to HCl and Cl⁻ should remain relatively constant for any given series of amines.

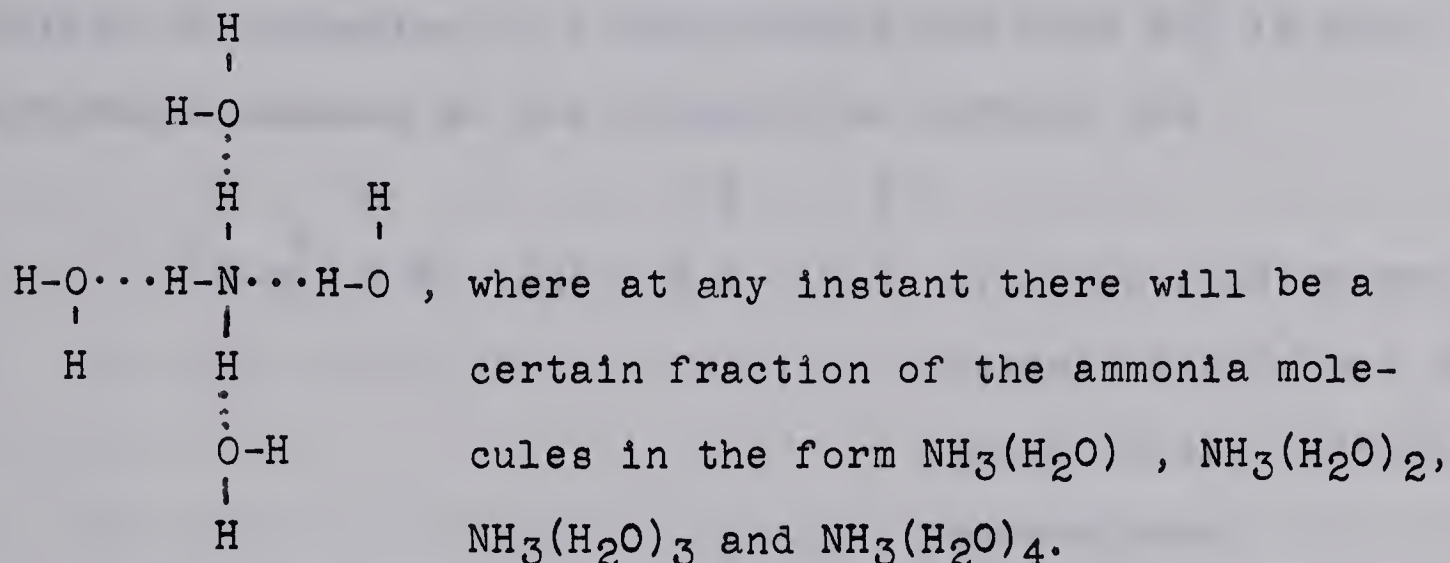
The solvation of ammonia can be considered as the

summation of the following structures.

1. Primary solvation



2. Secondary solvation



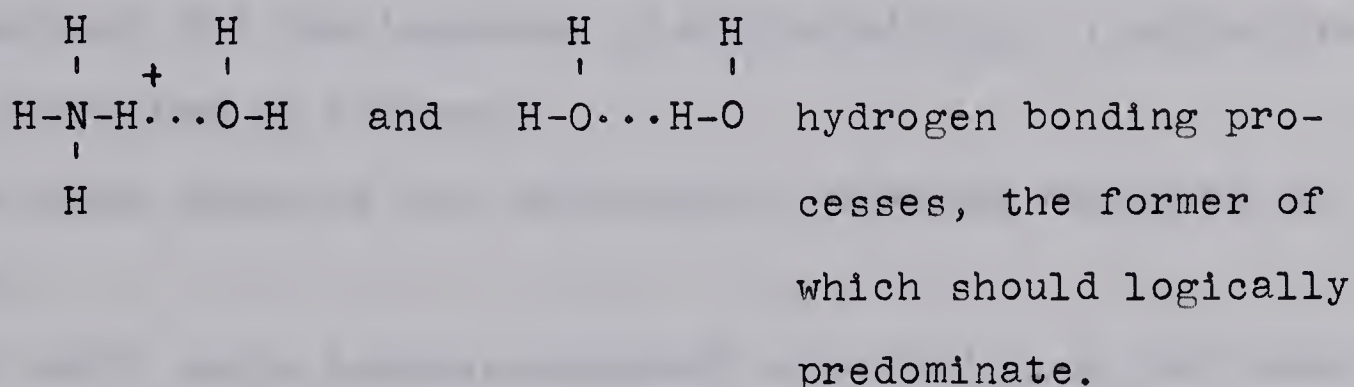
3. Tertiary solvation

As can be seen from the above structure, there are twelve sites still available for further hydrogen bonding by water. It is possible that further hydrogen bonding occurs so that species of the general formula $\text{NH}_3(\text{H}_2\text{O})_n$ are formed analogous to the solvated proton species postulated in dilute sulfuric acid (106, 107).

4. Cage structures

The solute molecule, NH_3 , or the primary solvated species may also be contained in a solvent cage, e.g. a dodecahedron, similar to that in the inert gas clathrates.

Upon protonation, the solvation of the ammonium ion takes a different form. The ion has four equivalent protons, each of which shares the positive charge. This fact limits the possible modes of hydration, i.e. there is no "primary" solvation, but probably enhanced "secondary" and "tertiary" solvation. If the $\text{NH}_4(\text{H}_2\text{O})_4^+$ species surrounded by a solvent cage was postulated, the cage would have to be made up of such a large number of water molecules, that the formation of such a cage would be statistically improbable. The possibility of formation of a cage around the bare NH_4^+ is also improbable because of the competition between the



Frank and Evans (5) have shown that, in general, ionic species show a net "structure breaking" effect on the solvent water as compared to uncharged species. For example, the standard entropy loss when a mole KCl is dissolved in water is $23.3 + 26.6$ e.u. whereas that of two gram-atoms of argon (the fairest comparison since both ions have the argon structure) is 2×30.2 e.u. The net effect, then, is that the ionic charges evidently reduce the entropy loss of solution, i.e. the solvent order is less than it would be in the presence of uncharged species'. It is therefore reasonable to postulate that a change in the order of the solvent in a protonation process will be manifested in an enthalpy change which is not accounted

for by non-solvation effects. It is also reasonable that the difference of solvation of one amine and its cation will not be the same as the difference of solvation of another amine and its cation. Thus the enthalpies of protonation will include different amounts of heat due to the solvation effect.

In the series of n alkyl amines there is an increase in the exothermicity of protonation as the alkyl chain is lengthened from one to six carbon atoms as illustrated in Figure 28. As has been previously pointed out, it is unlikely that this increase is solely due to the inductive effect but partially to a solvation effect. A solvation effect which would account for the increase in exothermicity, if operative, can be described as follows.

1. The amino group of the molecule is solvated similarly to ammonia.
2. The alkyl chain induces enhanced structuring of the water about it (in a manner reminiscent of clathrates) i.e. the alkyl group is a "structure maker" inducing cage or "ice-berg" formation.
3. Upon protonation, the charge on the amino group interferes with the solvent structure about the alkyl group, i.e. the solvation structure about the protonated amino group ("secondary" and "tertiary") is incompatible with the solvation structure about the alkyl group (cage). Thus the cage-like structure about the alkyl group would tend to be destroyed to a greater or lesser extent. As the length of the alkyl is increased, however, it would be expected that there would be a diminishing

effect on the solvation of the alkyl group (or on its "structure making" tendencies, which is an equivalent description of the same phenomenon) because of the increased separation of the two types of solvation on the same molecule. Thus there would be relatively fewer water to water hydrogen bonds broken when protonation occurs. The results would be an increase in exothermicity of amino protonation with increasing alkyl chain length.

In the series of *n* alkyl amines there is a steady decrease in the entropy of protonation (with the exception of ethylamine whose anomolous behaviour has previously been pointed out), i.e. the gain in entropy decreases from methylamine to *n* hexylamine. This is exactly what would be expected if the cage structure about the alkyl group could coexist with the cation solvation in the higher amines but not in the lower amines, i.e. breaking of solvent cages involves a gain in entropy.

No such increase in the exothermicity of amino protonation was found in the case of a series of amino acids, i.e. glycine, 2 alanine, 2 aminobutyric acid, norvaline and norleucine as is illustrated in Figure 32. The key difference in this series is that the carboxylate group has already contributed to this perturbing effect and upon protonation of the amino group the added interference ("structure breaking" effect) becomes unnoticable in terms of the enthalpy of protonation.

The most striking trend in evidence in any of the series' of compounds in this study is the large decrease in

exothermicity of protonation of the series of primary, secondary and tertiary amino groups. The series considered are

1. methylamine, dimethylamine, and trimethylamine
2. ethylamine, diethylamine, and triethylamine
3. n propylamine and di n propylamine
4. glycine, sarcosine, and NN dimethylglycine
5. ethylenediamine, N methylethylenediamine, and NN dimethylethylenediamine (including both the first and second protonation)
6. ethylenediamine, NN' dimethylethylenediamine, and NNN'N' tetramethylethylenediamine (including both the first and second protonation)

The trends are illustrated in Figure 29 by plotting the enthalpy of protonation as a function of the number of carbon atoms in each molecule and in Figure 35 by plotting the enthalpy of protonation as a function of the primary, secondary or tertiary character of each amino group. The striking similarity of the trends from series to series immediately suggests that a similar phenomenon is operative in all six series. As previously suggested solvation is thought to be the phenomenon responsible for these decreases in exothermicity of protonation with increased alkyl substitution on the amino groups.

An explanation which would account for the observed enthalpy results, is that in the secondary and tertiary amines there are fewer amino protons to take part in "secondary" solvation. For example, in the series methylamine, dimethylamine and trimethylamine the number of N-H...O hydrogen bonds possible

before protonation are 2, 1 and 0, respectively and after protonation are 3, 2 and 1, respectively. Each hydrogen bond existant before protonation would expected to be strengthened upon protonation due to the charge on the cation which would be shared by each of the amino protons. It is not unreasonable that such strengthening would involve an increased exothermicity of two to three kilocalories per mole per bond, which is sufficient to account for the difference in the observed enthalpy results.

This explanation, however, cannot account for the large differences in the entropies of protonation, e.g. for methylamine, dimethylamine and trimethylamine, the entropy of protonation was found to be 3.82, 7.41 and 14.8 e.u., respectively. In addition, it was found (see Table 15) that as the degree of N methyl substitution increased for the ethylenediamines, the heat of solution became more exothermic. The opposite would have been expected if the heat of solution was largely due to the formation of $\text{N-H}\cdots\text{O}$ hydrogen bonds. It would be expected that the solvation effect postulated above would be virtually independent for each of the amino groups of substituted ethylenediamines, but this was not found to be true. For example, the heat of protonation of one of the amino groups of NN dimethylethylenediamine should have been essentially the same as the corresponding heat of protonation of ethylenediamine but ΔH_1 was found to be 1.65 kilocalories per mole less exothermic and ΔH_2 was found to be 3.11 kilocalories per mole less exothermic.

The observed results, however, can be rationalized in terms of either complete or partial solvent cages around the amino groups. In the case of the smaller molecules, there is direct evidence that such cages do in fact exist and that at lower temperatures actual clathrate compounds do separate from aqueous solutions as solids (72, 108), where the water molecules form as dodecahedra or tetrakaidecahedra around the amine molecules. It would be expected that the tertiary amines would be the strongest "structure makers" since there is no possibility of "secondary" solvation and their greater "organic" character would tend to repel the solvent molecules to a greater extent forcing them into a cage formation, i.e. encystment of the amines by the water molecules would occur. Upon protonation, the ions formed would be net "structure breakers" and the breaking of water-water hydrogen bonds would result in a less exothermic heat of protonation since the breaking of hydrogen bonds would be an endothermic process. Thus the heat of protonation of a series of amines would be expected to be primary more exothermic than secondary more exothermic than tertiary.

The mean lifetime of such cage structures would of course be very short, perhaps in the order of 10^{-12} to 10^{-10} seconds but the mean "concentration" of cage structures (complete or partially complete) could be relatively high. Consider the series methylamine, dimethylamine and trimethylamine. Let us assume that no cages form around methylamine or the protonated amines, that the cages are dodecahedra, i.e. each

consists of twenty water molecules and thirty hydrogen bonds which have a heat of formation of five kilocalories per mole (the value in ice), that there are no partial cages formed, and that there is no factor other than cage formation causing differences in the enthalpies of protonation. It would then be necessary that less than 3% of the trimethylamine molecules and less than 0.7% of the dimethylamine molecules be surrounded by cages which are destroyed upon protonation to account for the differences in the enthalpy of protonation of this series of amines. The above assumptions are rather stringent, however, particularly the assumption that no partial cages exist. With partial cages present, i.e. either cages in the process of forming or breaking down, or "flickering" (104), the "concentration" of complete cages could be orders of magnitude less than that required under the above conditions.

The cage hypothesis would predict that the entropy of protonation would increase from primary to secondary to tertiary due to the increase in the translational entropy of the solvent molecules. This was found to be true for all of the series' studied as is illustrated in Figure 37. The entropy of protonation of the tertiary amines was particularly large, i.e. 14.8 for trimethylamine, 13.0 for triethylamine, 18.2 for NN dimethylglycine and 16.7 and 3.82 e.u. for the first and second protonation of NNN'N' tetramethylethylenediamine. The cage hypothesis is consistent with the successive entropy changes found for the protonation of the latter compound, i.e. it would be expected that the addition of the

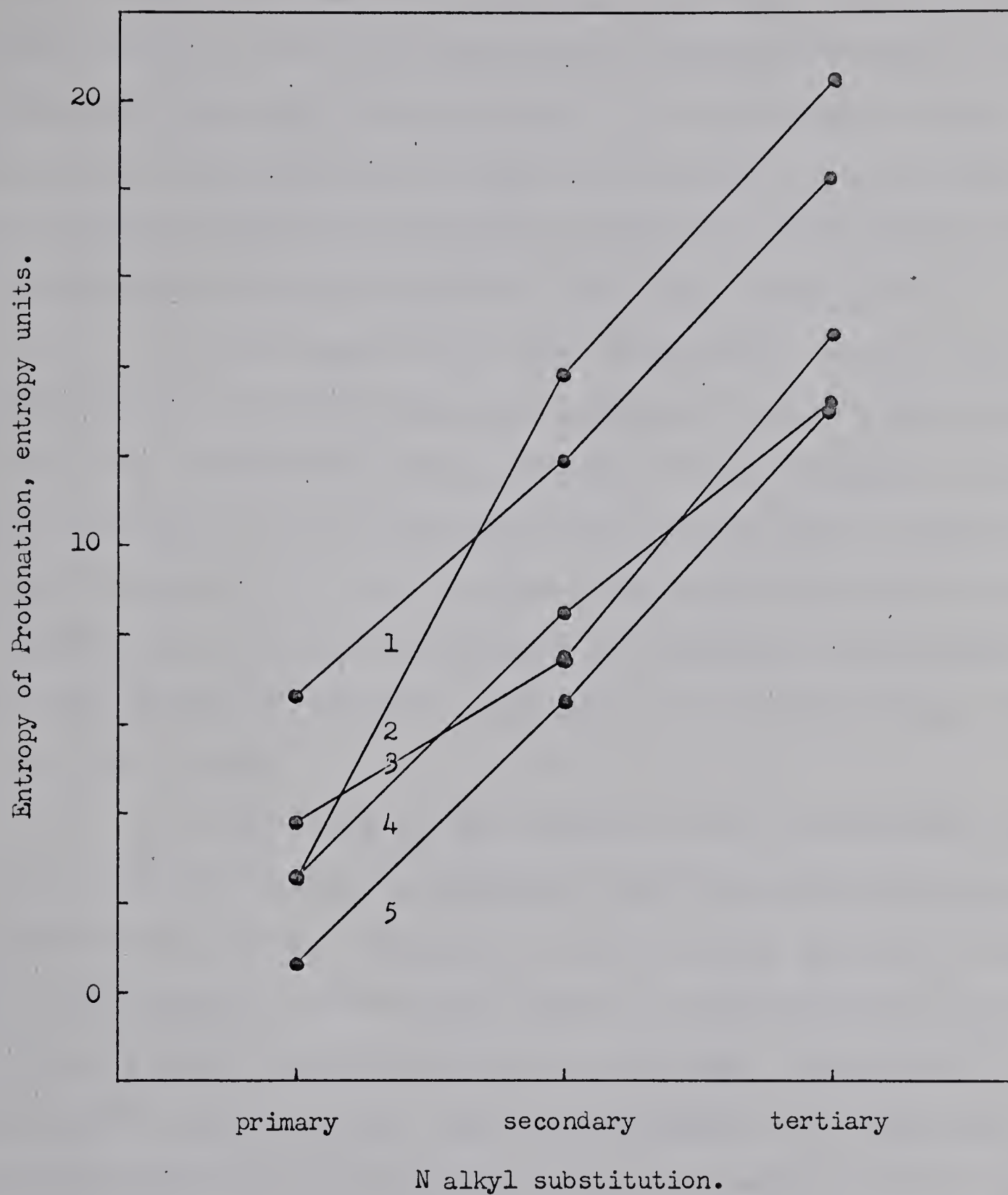


Figure 37. Entropy of protonation of primary, secondary and tertiary amino groups.

1. glycines
2. ethylenediamines, symmetrical methyl substitution, $\Delta S_1 + \Delta S_2$
3. methylamines
4. ethylenediamines, unsymmetrical methyl substitution, $\Delta S_1 + \Delta S_2$
5. ethylamines

first proton would destroy the cage about the first protonated amino group and that the now charged group would tend to interfere with the cage formation about the second amino group. Thus the first protonation would be expected to be accompanied by a rather large entropy change compared to the entropy change accompanying the protonation of the second amino group.

On the basis of the cage hypothesis, it would be expected that the series glycine, sarcosine and NN dimethylglycine would exhibit the least effects of cage formation because the solvation of the carboxylate group would tend to inhibit cage formation. In fact, it was found that the heats of protonation of this series exhibited the smallest differences of all the series of primary, secondary and tertiary amines studied in this work.

It was noted in the course of this study that there was a possibility that a specific solvation effect was operative: namely water bridging of the two amino groups of some of the diamines. The boiling points of ethylenediamine and ethylenediamine monohydrate are surprisingly similar 116° and 118°C , respectively. The distillates of the other diamines contained a considerable amount of water, albeit less than the 1:1 stoichiometric amount, but still boiled at temperatures very close to those reported in the literature for the pure compounds.

An attempt was made to determine whether or not 1:1 stoichiometry had any special significance by conducting a series of supplementary experiments. The supplementary

experiments indicated the existence of some form of diamine-water complex and in some cases the definite existence of 1:1 stoichiometry.

1. Heat of dilution. Figure 21.

The heat of dilution curves of three of the diamines studied took three forms. The dilution curve of ethylenediamine had an almost constant slope until the stoichiometric ratio of 1:1 had been attained and then the rise diminished as dilution was continued. This indicated the formation of a 1:1 species. The dilution curve of 1,4 diaminobutane took the form of a parabolic section which indicated no special significance of 1:1 stoichiometry. The dilution curve of NNN'N' tetramethylethylenediamine showed a much more gentle rise (at a mole ratio of 10:1 water to amine only about 70% of its total heat of dilution had been realized) which is consistent with the hypothesis of cage formation about the tertiary amines.

2. Heat of vaporization. Figure 22.

Evidence was found that indicated that 1:1 water-diamine species do indeed form in the water-NNN'N' tetramethylethylenediamine system.

3. Phase diagrams. Figure 23 and Figure 24.

There was definite proof found that the monohydrates of ethylenediamine and of NNN'N' tetramethylethylenediamine freeze out of the respective water-amine systems. Although this occurred at temperatures below 25°C, it does not seem unreasonable that such species should still persist at 25°

and even higher.

4. Gas chromatography. Figure 25.

It was found that the presence of amines affected the retention time of water (increased it) with the effect of diamines being greater than that of a monoamine having a similar boiling point.

5. Molecular weight determination.

An attempt was made to measure the molecular weight of a water-diamine system using the Victor Meyer method but no evidence of complex formation in the gas phase was found, i.e. the molecular weight found was the mean of the water and the diamine. It was necessary to use temperatures about 30°C above the boiling point of the amine so that lack of evidence of complex formation at elevated temperatures does not preclude its existence at lower temperatures and in the liquid phase.

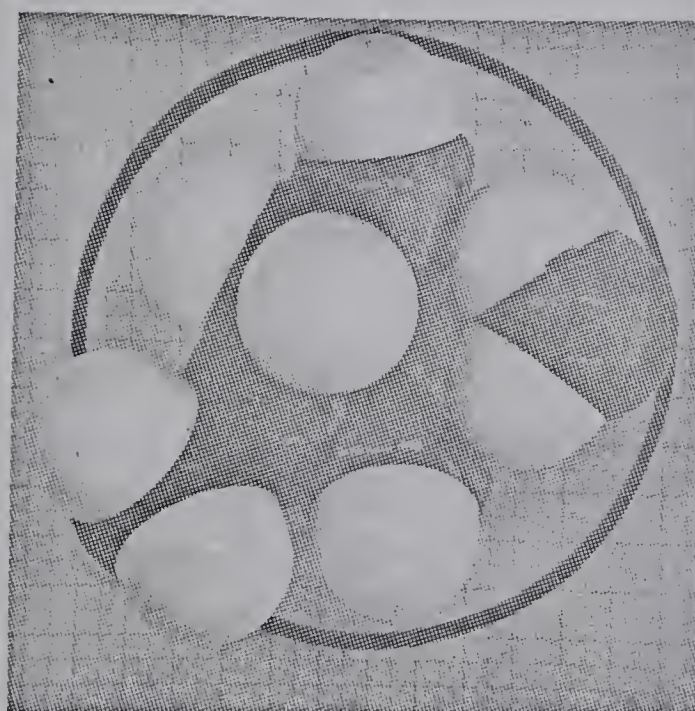
6. Nuclear magnetic resonance. Figure 26.

These studies indicated that a 1:1 water-diamine species formed in the systems 1,2 diamino-2-methylpropane-water and 1,4 diaminobutane-water. In the NNN'N' tetramethylethylenediamine-water system, there seemed to be first the formation of a 1:1 complex and then an indeterminate structure formation, possibly the formation of solvent cages about the amine.

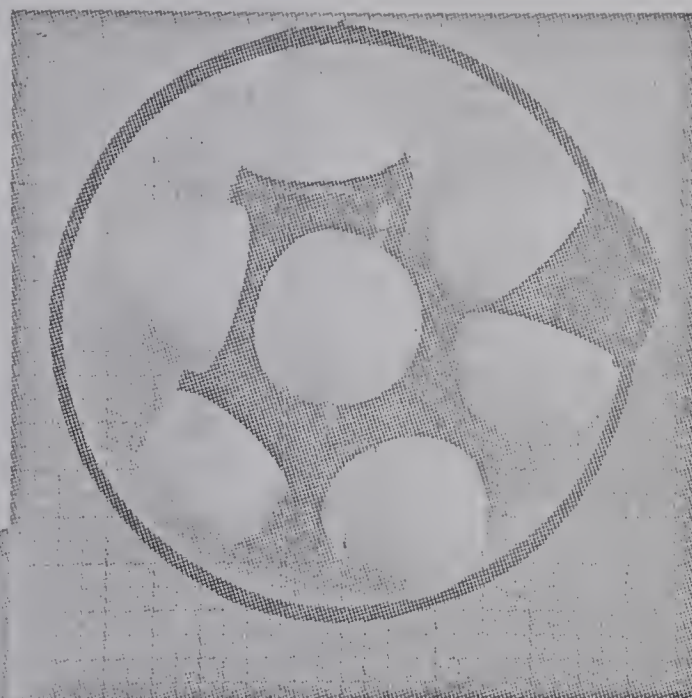
It would seem, in view of these experiments, that the formation of 1:1 water-diamine complexes does occur. These complex formations could, in fact, be regarded as chelate

structures, i.e. the diamine takes its usual role as the ligand and the water molecule takes the role of a metal ion as is shown in Figure 38. The stability of such a complex would of course be partially due to the favourable entropy effect (similar to the so-called entropy effect in the chelation of a metal ion). The complexes formed between water and the ethylenediamines would be five membered rings, excluding the two protons of water which would play a rather unimportant role in determining the steric stability of the species. The ring structure would be broken when the protonation of the first amino group takes place and there should be a relatively large gain in rotational entropy compared to that accompanying the second protonation. As the length of the alkyl chain separating the two amino groups in a series of diamines is increased the difference between ΔS_1 and ΔS_2 should diminish because the ring would be larger (Figure 29) and the larger the ring the less stable it would be expected to be (29, 109). This was found to be true for the series ethylenediamine, 1,3 diaminopropane and 1,4 diaminobutane, i.e. $\Delta S_1 - \Delta S_2$ values were found to be 7.41, 4.56 and 3.85 e.u., respectively.

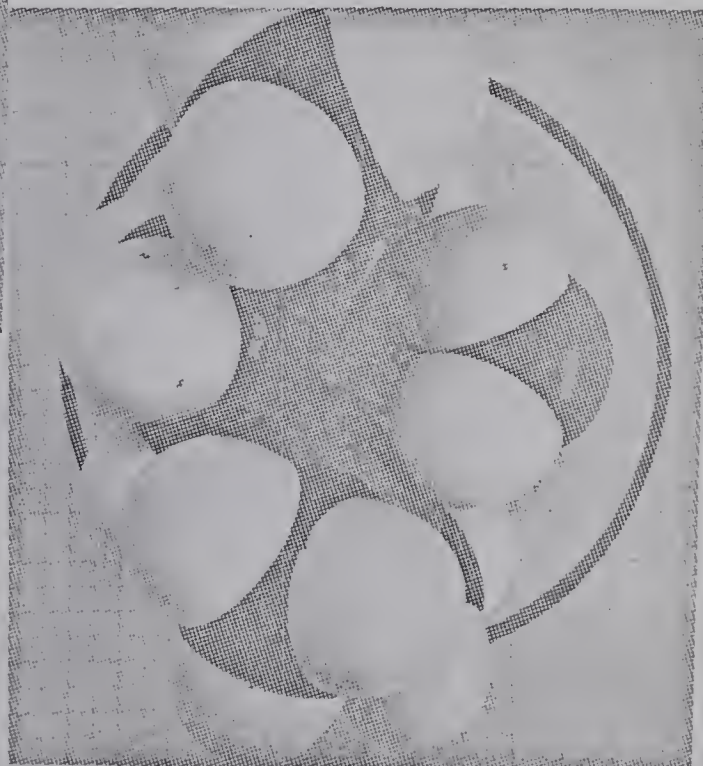
The existence of ring hydrates could account for the thermodynamic results reported by Ciampolini and Paoletti (98) for diethylenetriamine. They found $\Delta H_1 = -11.20$, $\Delta H_2 = -11.95$ and $\Delta H_3 = -7.20$ kilocalories per mole and $\Delta S_1 = 7.2$, $\Delta S_2 = 1.0$ and $\Delta S_3 = -4.7$ e.u. for the successive protonations of this triamine. The fact that ΔH_1 was found to be less exothermic and ΔH_2 was not expected but an explanation



1,2 diaminopropane

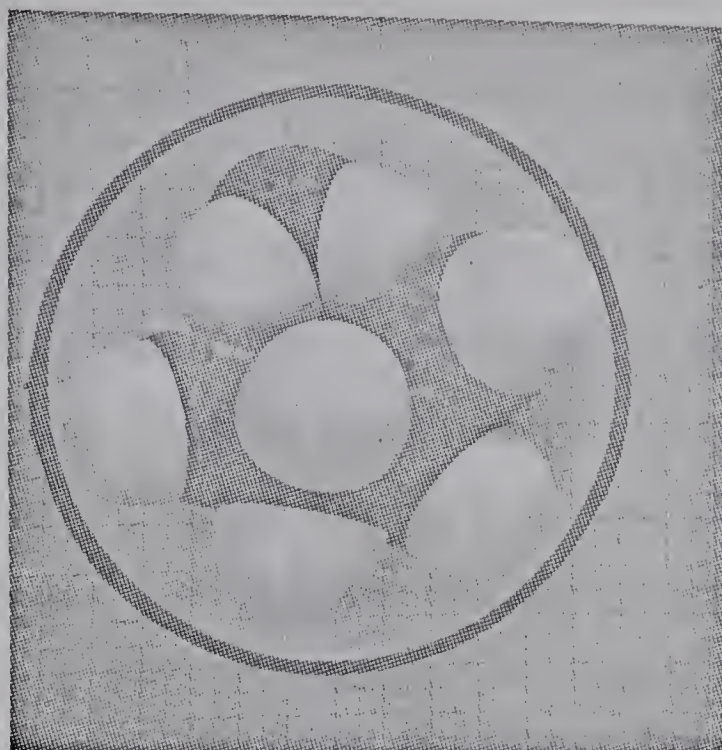


ethylenediamine

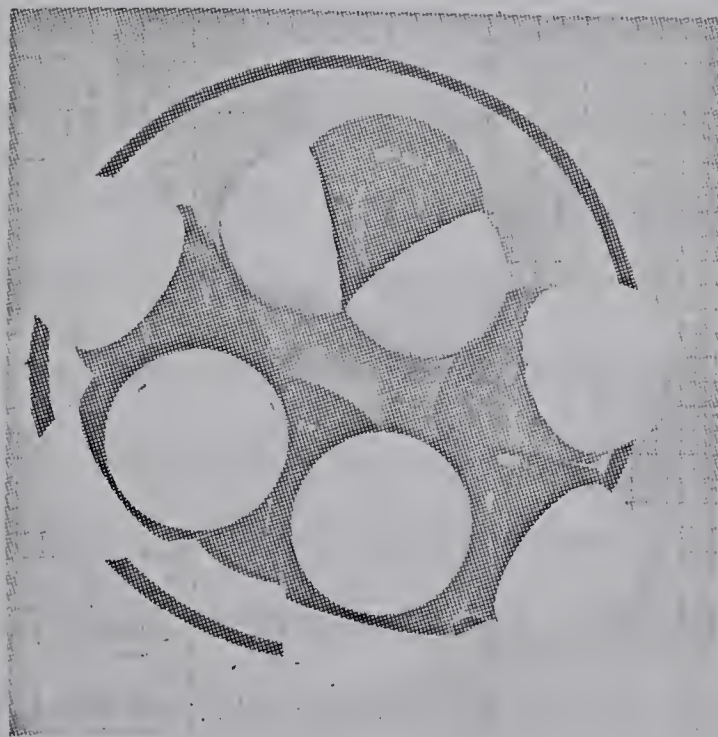


NNN'N' tetramethylethylenediamine

Figure 38. Monohydrates of ethylenediamines



ethylenediamine - water



1,4 diaminobutane - water

Figure 39. Diamine - water ring formation

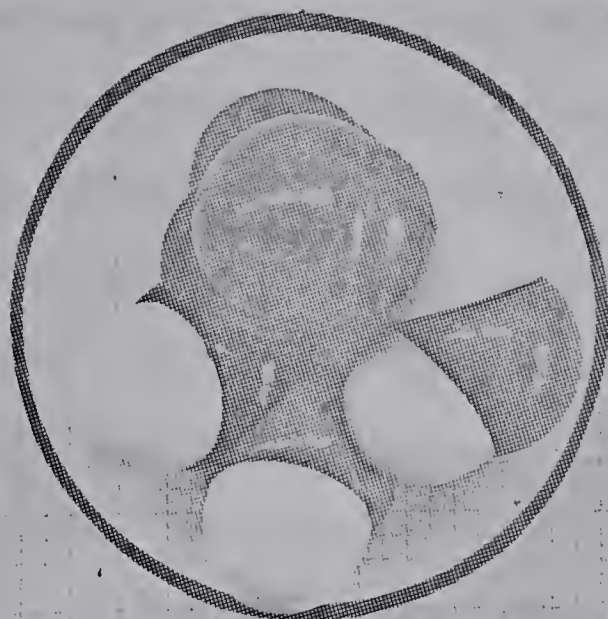
can be rationalized if ring formation occurs between the unprotonated amine and water. Any ring complex must involve the secondary amino group and only one of the primary amino groups. When the first protonation occurs, the site would be one of the primary amino groups. If it was the amino group involved in ring formation the ring would be destroyed and if it was the one not involved in ring formation, the presence of the charge would decrease the electron density on the other two amino groups so that the propensity to hydrogen bond would be diminished and the ring structure would at least be destabilized and probably be destroyed. Thus the first protonation would exhibit a less exothermic heat of protonation and a greater gain in entropy than would otherwise have been expected. The second protonation would not involve the dissociation of the water complex and thus could be more exothermic than the first protonation as was reported.

Interpretation of the thermodynamic results of the amino acids is more difficult because of the presence of the two functional groups. As has already been pointed out, there is likely intramolecular hydrogen bond formation which would affect the thermodynamics of both the amino and carboxylate protonations. In general, it would seem that for the α amino acids, intramolecular hydrogen bonding of the zwitterion would be increased as substitution on the α carbon atom was increased, i.e. as the molecules became more "organic" the polar solvent would "force" the molecule into intramolecular hydrogen bond formation. This phenomenon would result in

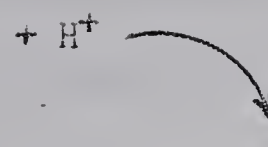
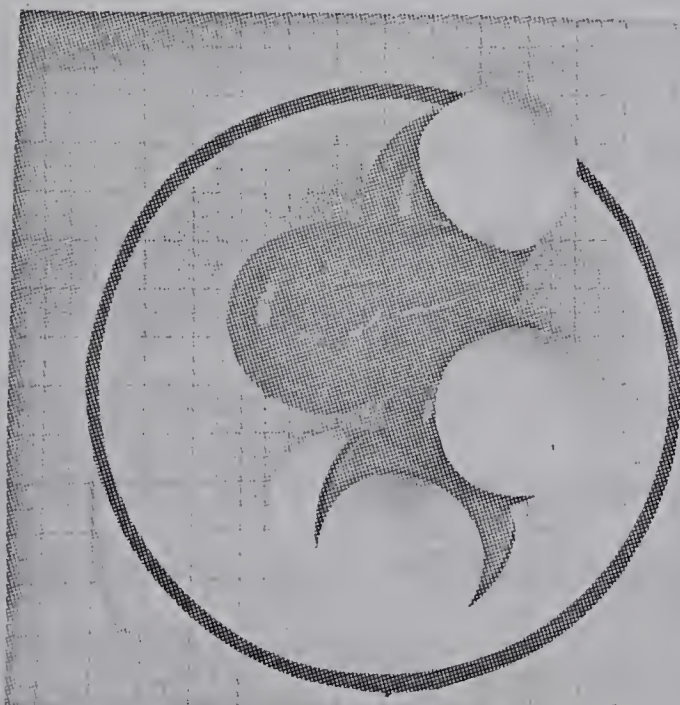
more exothermic heats of protonation and decreased entropies of protonation of the amino group, and less exothermic heats of protonation and increased entropies of protonation of the carboxylate group as the side chain increased in length. In general the latter effect was found but not the former so that it is dangerous to speculate on the importance of this factor.

The possibility of hydrophobic bond formation (110) must also be considered but its effects would be similar to those expected in the presence of intramolecular hydrogen bond formation. The manner in which this could occur would be by intermolecular hydrogen bonding of the ammonium group of one molecule to the carboxylate group of a second molecule and alignment of the alkyl side chains due to mutual attraction (or repulsion by the polar solvent). With the data available, it is not possible to speculate on the importance or even the existence of hydrophobic bond formation.

The amino acid anion could possibly form a ring species similar to that postulated for the diamines with water. This would cause a decrease in the enthalpy of amino protonation of a series of α amino acids as the length of the side chain increased. This decrease could be offset by an increase due to intramolecular hydrogen bond formation and or hydrophobic bond formation. That is, if the process illustrated in Figure 40 occurred, the heat of protonation of the amino group would tend to remain more or less constant, the heat of protonation of the carboxylate group would tend to



anion (water bridged)

zwitterion (intramolecularly
hydrogen bonded)

cation (solvated functional groups)

Figure 40. The protonation of glycine.

become less exothermic, the entropy of protonation of the amino group would initially increase then decrease as intramolecular hydrogen bonding (or hydrophobic bonding) became more important and the entropy of protonation of the carboxylate group would steadily increase as the side chain increased in length and complexity. Since this was approximately the situation found, the process illustrated in Figure 40 seems to be fairly reasonable.

The conclusion drawn from this discussion is that solvation effects are very important in determining the thermodynamics of protonation of the compounds studied. The main solvation effect is due to the formation of solvent cages or "iceberg" structures about the "organic" portions of the molecules, this type of formation being most important about the unprotonated species, i.e. the unprotonated species are "structure makers". When protonation occurs these ordered structures are destroyed to a greater or lesser extent, i.e. the protonated (or charged) species are "structure breakers". These effects along with other special solvation effects affect the thermodynamics of protonation of amino groups to a rather large degree with the free energy term being more or less unaffected but with enthalpy and entropy terms showing the greatest fluctuations.

C. Metal Complexes.

Since the formation of metal complexes with a particular ligand is more or less analogous to the protonation of that ligand, there should be some relationship between the stability of the complexes formed between a metal ion and a series of similar ligands and the thermodynamics of protonation of those ligands. Bjerrum (111) has compiled the data of many investigators in such a manner as to emphasize the rather good correlation of the proton affinity (measured by pK_a) of particular ligands and their tendency to form complexes with metal ions. On this basis it would be expected that all of the alkyl monoamines studied in this work should form more stable complexes with metal ions than does ammonia and that some ligands with increased alkyl substitution on the nitrogen should form more stable complexes than the primary amines. However, many investigators have found that this is not the case (112).

In the case of the diamines, a decrease in the stability of complexes with increased alkyl substitution has been interpreted as being mainly due to steric factors (28, 35, 95). The role of solvation effects, however, has not, in our opinion, been given adequate scrutiny. In view of the rather important role of solvation effects described in this study, it would seem that such solvation effects should also play an important role in determining the stability of coordination compounds in aqueous solution. Since it has been shown that the free energy of protonation is a poor measure

of these effects, it might be advantageous to compare enthalpy of protonation data and the stability constants of metal coordination compounds.

In Figure 41 the logarithms of the overall stability constants are plotted as a function of the heats of protonation of the ligands, i.e.

1. $\log \frac{[\text{AgL}^+]}{[\text{Ag}^+][\text{L}]^2}$ versus ΔH_L , where L represents a monoamine.
2. $\log \frac{[\text{CuL}_2^{++}]}{[\text{Cu}^{++}][\text{L}]^2}$ versus $(\Delta H_1 + \Delta H_2)_L$, where L represents a diamine.
- 2a. $\log \frac{[\text{CuL}^{++}]}{[\text{Cu}^{++}][\text{L}]}$ versus $(\Delta H_1 + \Delta H_2)_L$
3. $\log \frac{[\text{CuL}_2]}{[\text{Cu}^{++}][\text{L}]^2}$ versus $(\Delta H_1 + \Delta H_2)_L$, where L represents an amino acid.

The values of the logarithms of the stability constants at 25°C were selected from references 10 and 11 and 97. The metal ions used in Figure 41 are those for which the most data has been reported but other metals exhibit similar trends. As can be seen from Figure 41, there is a direct relationship between the heats of protonation of the monoamines and the diamines and the stabilities of the complexes formed with these molecules as ligands. The relationship is not so apparent in the case of the amino acids but this is not unexpected since neutral complexes are formed which complicates any interpretation of the results.

Since the enthalpy of protonation of both classes of amines are strongly influenced by solvation effects and the stability of the complexes seem to be directly proport-

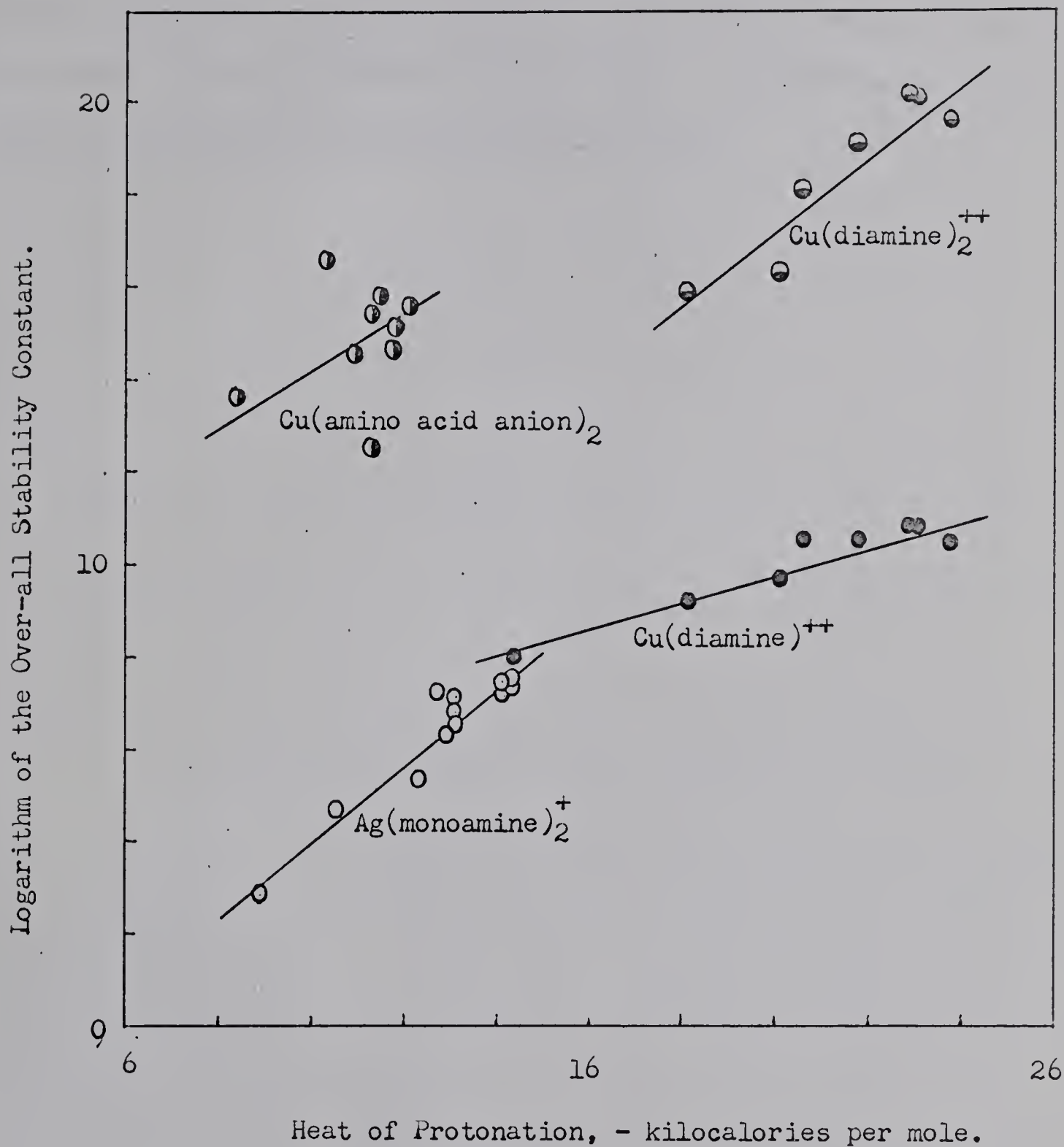


Figure 41. Dependence of the stability of metal complexes upon the heat of protonation of the ligands.

ional to the exothermicity of protonation of the amines, it would not be unreasonable to conclude that the stability of the complexes is affected to a greater or lesser extent by the same solvation effects which would surely be also operative as the amines complex the metal ions.

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